PERGAMON

European Journal of Cancer 36 (2000) 207–213

European Journal of Cancer

www.elsevier.com/locate/ejconline

Non-Hodgkin's lymphoma presenting with spinal cord compression; a clinicopathological review of 25 cases

A.C. McDonald[a,*], J.A.R. Nicoll[b], R.P. Rampling[a]

[a]*University Department of Radiation Oncology, Beatson Oncology Centre, Western Infirmary, Glasgow G11 6NT, UK*
[b]*University Department of Neuropathology, Institute of Neurological Sciences, Southern General Hospital, Glasgow, UK*

Received 26 February 1999; received in revised form 6 September 1999; accepted 12 October 1999

Abstract

The aim of this study was to retrospectively examine 25 patients with newly diagnosed non-Hodgkin's lymphoma (NHL) presenting with spinal cord or cauda equina compression as the first symptom that were referred to our department between 1985 and 1996. At presentation 17 patients were non-ambulatory; dual sphincter impairment was found in 9 patients with a further 8 patients having bladder dysfunction only. All patients had a tissue diagnosis. Five low-grade and 20 intermediate or high-grade tumours were identified. In this latter group 4 patients were treated palliatively and the remaining 16 patients received combination chemotherapy and/or radical radiation therapy. The overall survival at 5 years is 59%. The majority of patients became ambulatory, even if paretic at presentation. This is in marked contrast to reports of patients presenting in this fashion due to metastatic carcinoma. We urge this diagnosis be considered in all patients presenting with spinal cord compression attributed to malignancy.

Keywords: Non-Hodgkin's lymphoma; Spinal cord compression

1. Introduction

Myelopathy secondary to malignant epidural spinal cord compression is common in both neurosurgical and oncological practice. In epithelial tumours it usually occurs in the later disease stages, with most patients failing to survive more than 6 months from the onset of neurological dysfunction [1,2]. Less frequently patients may present with signs of cord compression as an initial manifestation of malignancy. In patients with non-Hodgkin's lymphoma (NHL), such primary presentation with myelopathy is rare and thought to occur in less than 5% of cases [3–8]. Even in major centres experience of this entity is modest and optimal treatment thus remains unclear. The literature base largely comprises small retrospective series and single case reports [9–19]. We reviewed departmental records covering the 11-year period from 1985 to 1996 and identified 25 patients presenting with spinal cord compression as their first manifestation of NHL. We describe the findings of this analysis which represents one of the largest single-centre series in the modern literature.

2. Patients and methods

2.1. Clinical features

Clinical characteristics of the 25 patients described are detailed in Tables 1 and 2. Motor and sphincter function are detailed in Table 3. All patients presented with neurological impairment, usually a mixed sensorimotor deficit. Back pain of variable duration (median 3 months; range: 3 days–18 months) preceded acute neurological presentation in 18 patients. 17 patients experienced sphincter disturbance at diagnosis; each had bladder dysfunction (requiring urethral catheterisation). 9 patients also had anal sphincter disturbance (lax sphincter tone on digital examination or faecal incontinence).

Motor function was assessed retrospectively by case-sheet review and graded 1–4 as detailed in Table 3. A separate assessment of performance status was not made, given the importance of mobility in its estimation. At

* Corresponding author. Tel.: +44-141-211-1744; Fax: +44-141-211 6356.
E-mail address: amcdonald@wghut-nhs.org.uk (A.C. McDonald).

0959-8049/00/$ - see front matter
PII: S0959-8049(99)00265-8

presentation 17 patients had grade 1–2 mobility whilst 8 patients had grade 3–4. Referral was in most instances via the regional neurosurgical centre (23 pts). Extradural spinal cord compression was confirmed radiologically in 12 patients using myelography; with or without computerised tomography (CT). In the remainder, the level of compression was determined by non-contrast assisted CT (2 pts) or spinal magnetic resonance imaging (MRI) (11 pts). The thoracic region was the most common disease site (17 cases). Other sites were cervical (2 pts), cervico-thoracic (1 pt), lumbar (4 pts), or sacral (1 pt). 16 patients underwent posterior laminectomy and tumour debulking, 2 undergoing a concomitant stabilisation procedure. 8 patients had spinal tumour biopsy alone. The remaining patient underwent cervical lymph node biopsy. No patient deteriorated neurologically in the immediate post-operative period.

2.2. Histopathological evaluation

Histological sections from 20 cases for which archived material was available have been reviewed (JARN) and confirmation of lymphoid malignancy obtained in each. Further sub-classification of 9 of these cases was performed by one of several lymphoma pathologists who had also assessed the remaining five tumours. Histological grading was assessed using the working formulation (WF). Initial diagnostic material, whether obtained by surgical decompression or needle biopsy was frequently small in size and subject to crush artefact; these factors precluded accurate WF sub-classification of many of the diffuse lesions.

Additional material obtained by lymph node biopsy in 5 cases produced a revision of diagnosis in 1 patient (initial biopsy suggesting an undifferentiated neoplasm, subsequently categorised as an intermediate grade NHL on review) and revision of WF grade (from intermediate to low-grade) in 2 cases. In 11 patients tumours were impossible to fully grade; these cases exhibited no features of low-grade disease and are included within the intermediate/high-grade tumour category for the purposes of analysis. Of the remaining 14 cases, 5 high-grade, 4 intermediate and 5 low-grade tumours were identified. Immunocytochemical studies using standard antibodies on paraffin sections were carried out in 24 cases; 18 cases displayed immunoreactivity with B-cell markers and 4 had immunophenotypic features of T-cell

Table 1
Clinical characteristics of patients with intermediate/high-grade disease

	Age (years) (sex)	Level	Mobility score[a]	Sphincters B/A[b]	Stage	Local extent[c]	Pathology (ICC)[d]	WF Grade[e]	Treatment No. 1	Response and outcome[f]	Survival and status[g]
1	66 (f)	T2	1	−/−	1e	B + PS	D (B)	Int/high	RT	PD	1: DNDF
2	71 (m)	C4–T2	1	−/−	1e	PED	D (B)	Int/high	RT + CHOP	PD	2.5: DNDF
3	73 (m)	T8–9	2	+/+	1e	PED	DCB (B)	Int	RT	CR	3: DDF
4	61 (f)	T3–5	2	−/+	1e	PED	D (B)	High	CHOP + RT	CR	24: ADF
5	52 (f)	L1	4	+/+	1e	B + PS	D (B)	Int/high	CHOP + RT	CR	24: ADF
6	72 (f)	L2	2	−/+	1e	B + PS	D (B)	Int/high	RT	CR	35: ADF
7	46 (m)	T4	1	+/+	1e	PS	D (B)	Int/high	VAPEC-B + RT	CR→Rec	36: ADF
8	65 (m)	T2	2	−/+	1e	B	D (B)	Int	CHOP + RT	CR	38: ADF
9	68 (f)	T5–7	3	−/−	1e	PED	D (B)	Int/high	RT	CR	51: ADF
10	62 (f)	C5–T1	1	−/+	1e	PED	D (B)	Int/high	RT	CR	63: ADF
11	54 (m)	C1–C3	1	−/−	2a	B + PS	D (−ve)	Int/high	VAPEC-B + RT	CR	13: ADF
12	72 (f)	Sacrum	3	+/+	4a	B + PS	D (B)	Int/high	CHOP	PR	2: DNDF
13	16 (m)	T6–8	1	−/−	4a	PED	DLB (B)	High	See text	CR	32: ADF
14	17 (f)	T6–8	2	−/+	4a	PED	DLB (B)	High	CHOP	CR	41: DDF
15	31 (m)	T6–8	2	+/+	4b	B + PS	LCAL (T)	High	See text	CR	46: ADF
16	40 (m)	T12	2	−/+	4a	B	D (T)	Int/high	RT + VAPEC-B	CR→Rec	64: ANDF
17	78 (f)	T4–8	1	−/−	3a	B + PS	DCB (B)	Int	RT	PD	1.5: DNDF
18	40 (m)	T8	1	−/−	3a	PS	D (T)	High	RT + CT	PR	1.5: DNDF
19	51 (f)	T3–4	1	−/−	4a	B + PS	D (T)	Int/high	RT	PD	1: DNDF
20	72 (m)	T3–5	2	−/−	4a	PS	DCB (−ve)	Int	CHOP	PR	4: DNDF

CHOP, cyclophosphamide/doxorubicin/vincristine/prednisone; VAPEC-B, vincristine, doxorubicin, prednisolone, etoposide, cyclophosphamide-bleomycin; RT, radiotherapy; f, female; m, male.

[a] Mobility score: 1, complete paraplegia; 2, paraparesis precluding weight bearing/mobilisation; 3, mild paraparesis, mobile with aids or assistance; 4, independent mobility without aids or assistance.

[b] Sphincters normal (+) or abnormal (−) sphincter function. B, bladder; A, anal.

[c] Local extent: B, bone destruction; PS, paraspinal mass; PED, primary extradural deposit.

[d] Pathology: D, diffuse lesion; DCB, diffuse centroblastic; DLB, diffuse lymphoblastic; LCAL, large cell anaplastic tumour; ICC, immunocytochemical staining; B, positive staining with B-cell markers; T, positive staining with T-cell markers.

[e] WF, Working formulation grade. Int/high, diffuse tumours with no features of low-grade disease; Int, intermediate grade tumours.

[f] Response/outcome: CR, complete response; Rec, recurrent disease; PR, partial response; PD, progressive disease.

Table 2
Clinical characteristics of patients with low-grade disease

	Age (years) (sex)	Level	Mobility score[a]	Sphincters B/A[b]	Stage	Local extent[c]	Pathology (ICC)[d]	Treatment No. 1	Response and outcome[e]	Survival and status[f]
21	50 (m)	L3–5	4	+/+	1e	PED	DL (B)	RT (40 Gy/20#)	CR→Rec	84 mo: ADF
22	55 (f)	T12	3	−/+	1e	B	DL	RT (32.4 Gy/12#)	CR	103: ADF
23	49 (f)	T11	3	−/+	1e	PED	FCC (B)	RT (34 Gy/10#)	CR→Rec	110: ANDF
24	64 (f)	L4–5	3	+/+	4a	B+PS	FM (B)	CT (CHOP)	CR→Rec	133: ANDF
25	67 (f)	T10–12	4	+/+	4a	B	FCC (B)	RT (35 Gy/20#) + chlorambucil	PR	20: ANDF

CHOP, cyclophosphamide/doxorubicin/vincristine/prednisone; RT, radiotherapy.

[a] Mobility score: 1, complete paraplegia; 2, paraparesis precluding weight bearing/mobilisation; 3, mild paraparesis, mobile with aids or assistance; 4, independent mobility without aids or assistance.

[b] Sphincters normal (+) or abnormal (−) sphincter function. B, bladder; A, anal.

[c] Local extent: B, bone destruction; PS, paraspinal mass; PED, primary extradural deposit.

[d] Pathology: D, diffuse lesion; DL, diffuse lymphocytic; F, follicular lesion; FCC, follicular centrocytic; FM, follicular mixed. ICC, immunocytochemical staining; B, positive staining with B cell markers.

[e] Response/outcome: CR, complete response; Rec, recurrent disease; PR, partial response.

[f] Disease status; A, alive; D, dead; (N)DF, (non)-disease-free.

neoplasms; immunostaining was unhelpful in the remaining 2 cases.

2.3. Disease staging

Disease staging was carried out using CT scanning and bone marrow biopsy. Cerebrospinal fluid was not routinely evaluated, but was negative in the 4 cases where it was sampled. No significant haematopoietic, renal or metabolic abnormalities were identified in any patients apart from 2 with a heavy disease burden, who had reduced serum albumin. Serum lactate dehydrogenase (LDH) was not routinely measured. Antibody testing for the Human Immunodeficiency Virus (HIV) was not routinely performed, although 2 patients developed lymphoma as a sequelae to HIV infection.

Tumour characteristics are shown in Tables 1 and 2. Tumours were localised in 13 cases and more widespread in the remainder. Local tumour extent was divided into four groups: (i) tumours of primary bone origin, causing vertebral destruction (4 pts); (ii) paravertebral tumours with extension into the spinal canal (3 pts); (iii) tumours with bony vertebral destruction and an associated paravertebral mass (9 pts); (iv) tumours with neither bone destruction nor a paravertebral mass (9 pts). 7 patients within this latter group had no disease demonstrable in other sites and thus had disease of primary extradural origin.

2.4. Treatment

2.4.1. Intermediate and high-grade tumours

Treatment details are summarised in Tables 1 and 2. 16 patients (pts 1–16) with intermediate/high-grade disease were treated radically. 9 patients within this group initially received chemotherapy using either a 3-weekly cyclophosphamide, doxorubicin, vincristine, prednisolone (CHOP) regimen (5 pts; median of four courses received: range: 2–6) or the vincristine, doxorubicin, prednisolone, etoposide, cyclophosphamide-bleomycin (VAPEC-B) combination, (4 pts, all completing 12 weeks) an alternating weekly regimen delivered in 12 courses [20].

2 of these patients, both with high-grade stage 4 disease (bone marrow involvement), received additional dose-intense therapy following remission induction with VAPEC-B. Patient 13 (B cell lymphoblastic lymphoma) received high-dose methotrexate central nervous system (CNS) prophylaxis, followed by total body irradiation (TBI; 1440 cGy in 8 fractions over 4 days) and high-dose cyclophosphamide (3.6 g/m^2) delivered with progenitor cell support. Patient 15 (high grade T cell tumour, with B symptoms), received three cycles of intrathecal methotrexate with VAPEC-B, followed by TBI and high-dose cyclophosphamide as above.

Of the 7 other patients receiving initial chemotherapy, 5 patients received consolidation radiotherapy to the site of initial disease following a complete response to treatment. Doses (36–45 Gy in 1.8–2 Gy per fraction, using 4–6 MV photons) were prescribed at spinal cord depth in accordance with ICRU 50. The remaining 2 patients (pts 12 and 14) both had stage 4 disease at presentation and received chemotherapy only.

7 patients were treated initially with radiotherapy alone. This choice of treatment was based on doubts over individual patient tolerance of cytotoxics, although 2 patients (pts 2 and 16) subsequently received chemotherapy. The remaining 5 patients, (pts 1, 3, 6, 9 and 10, all with stage 1 disease) were treated exclusively with radiotherapy, each receiving 40 Gy in 20 fractions.

4 patients (pts 17–20), unfit for radical treatment, received palliative treatment only; 3 patients with extensive disseminated disease, total paraplegia and dual sphincter impairment received palliative spinal radiotherapy. All 3 patients died within 6 weeks of diagnosis. The fourth, an HIV positive male received palliative radiation and chemotherapy (vincristine and bleomycin).

Table 3
Motor and sphincter function at presentation, 1 and 6 months from diagnosis

Time after presentation		Motor function		Bladder function		Anal sphincter	
	n	Grade 1–2	Grade 3–4	Normal	Abnormal	Normal	Abnormal
Presentation	25	17	8	8	17	16	9
1 Month	24	7	17	15	9	20	4
6 Months	17	1	16	16	1	17	0

Mobility score: 1, complete paraplegia; 2, paraparesis precluding weight bearing/mobilisation; 3, mild paraparesis, mobile with aids or assistance; 4, independent mobility without aids or assistance.

2.4.2. Low-grade tumours

5 patients presented with low-grade disease (pts 21–25, detailed in Table 2). 3 patients with stage 1 disease received radical radiotherapy (32–40 Gy in 2–2.7 Gy per fraction). The remaining 2 patients had bone marrow involvement at diagnosis; 1 (pt 24) received six cycles of CHOP chemotherapy. The second, (pt 25) was treated with radiotherapy and chlorambucil. Both have received further local and systemic treatment in palliation.

3. Results

3.1. Intermediate/high-grade tumours treated with chemotherapy

11 patients with non-low-grade disease were managed radically with cytotoxics with or without additional radiation. 2 patients have developed recurrent disease after 30 (pt 7) and 53 (pt 16) months respectively. Neither recurred locally. Both had received local radiotherapy. Patient 16 had sustained a (non-disease related) cerebrovascular accident 3 years before disease recurrence and was not fit for further aggressive therapy. He received palliative cytotoxics (cyclophosphamide, vincristine and prednisolone).

Patient 7 relapsed in the left groin (biopsy confirmed) 26 months after completing initial chemotherapy and was successfully salvaged with a 3-weekly combination of ifosfamide (3 g/m^2) and cytosine arabinoside (800 mg/m^2 days 1 and 8) for four courses, achieving a complete response. He underwent high-dose consolidation with carmustine (BCNU) 300 mg/m^2 day 1; etoposide 300 mg/m^2 and cytosine arabinoside 200 mg/m^2 both days 1–4 and melphalan 140 mg/m^2 day 5) given with stem cell support. He remains alive and disease free 30 months following completion of treatment.

3 patients in this group have died; patient 14 developed neurological complications associated with HIV infection 2 years after completing treatment, with no evidence of recurrent lymphoma. Patient 12 died from neutropenic sepsis and patient 2 died 6 months after chemotherapy was abandoned due to deteriorating general condition.

3.2. Intermediate/high-grade tumours treated with radical radiation alone

5 patients with non-low-grade tumours were treated with radical radiotherapy. 2 (pts 1 and 3) have died from acute cardiopulmonary events within 3 months of treatment completion. It should be emphasised this treatment modality was chosen due to the poor general condition of these patients. 3 patients are alive although patient 9 relapsed systemically after 2 years. She was successfully salvaged with combination chemotherapy (CHOP, six cycles) and remains alive and disease free 19 months after completing treatment.

Overall, of the 16 patients managed radically, 11 are alive and 10 disease free after a median follow-up of 36 months (range: 12–63).

3.3. Low-grade tumours

All patients with low-grade disease remain alive after a median follow up of 8.5 years (range: 20–133 months). Of the 3 patients with stage 1 disease treated with radical radiotherapy (pts 21, 22 and 23), 2 patients subsequently relapsed after 3 and 6 years. Patient 21 relapsed in the right supraclavicular fossa, biopsy revealing transformation to a high-grade tumour. He received chemotherapy (CHOP, six cycles) followed by consolidation radiotherapy and remains alive and disease free 25 months following completion of treatment. Patient 23 has received chemotherapy and radiation in palliation. The 2 remaining cases, with stage 4 disease at presentation have exhibited a typical low-grade pattern of relapse/remission and have been treated with a variety of cytotoxics and radiation in palliation.

3.4. Functional outcome

Mobility at presentation is shown in Table 3. The majority (17 patients) exhibited moderate or severe functional impairment at presentation, precluding independent mobility. One month after presentation 9 patients had improved to grades 3 or 4.

Initial paraplegia was a poor indicator of final functional outcome. 9 patients had grade 1 mobility at presentation; 5 of this group were dead within 6 months of

diagnosis despite substantial improvement in function in 2. Of the remainder, 3 regained mobility in the 6 months after diagnosis. The fourth became independently mobile by 2 years.

18 patients had either bladder dysfunction at presentation (8 pts) or dual sphincter problems (9 pts). The latter was predictive of poor prognosis, with 6 of the 9 doubly incontinent patients dead 6 months after diagnosis. Return of both bladder and bowel function was seen in 2 remaining patients by 6 months and by 2 years in the third. 9 patients with bladder dysfunction alone survived the initial 6-month period and regained bladder control during this time.

3.5. Survival and prognostic factors

Survival analysis was carried out using the Kaplan–Meier method with survival rate comparisons performed using the Mantel–Cox test. Death rate ratios and associated confidence intervals were obtained from the corresponding Cox proportional hazards model. The overall survival at 5 years was 59% (Fig. 1). Univariate analysis of potential prognostic factors of patient age, disease stage, WF grading (low-grade versus intermediate or high), presence of bone destruction and surgical procedure performed (decompression versus biopsy alone) showed no statistically significant association with survival. An effect was demonstrated for patient mobility scores (1 versus 2–4; death rate ratio 1:2–4 = 0.27, 90% confidence interval (CI) = 0.07–1.04, $P = 0.040$) and the presence of anal sphincter dysfunction (death rate ratio dysfunction absent:dysfunction present = 0.17, 95% CI = 0.04–0.68, $P = 0.004$). However, the small patient numbers severely limit the emphasis which can be placed on these observations precluding an adequate univariate analysis of prognostic factors.

4. Discussion

Spinal cord compression (SCC) is an uncommon primary manifestation of NHL, occurring in less than 5% of newly diagnosed cases [3–8]. Published series are small and retrospective [3,9–11,13,14,18,19,21] with few detailing more than 20 cases [12,16,22]. SCC occurring as a complication of disseminated NHL is more common and some authors combine such cases with those presenting with SCC [23,24]. We describe 25 patients, one of the largest of modern reports. Contrary to some [9,22] we do not exclude patients with extraspinal disease, but focus on the clinical aspects of the management of patients presenting with SCC due to undiagnosed NHL.

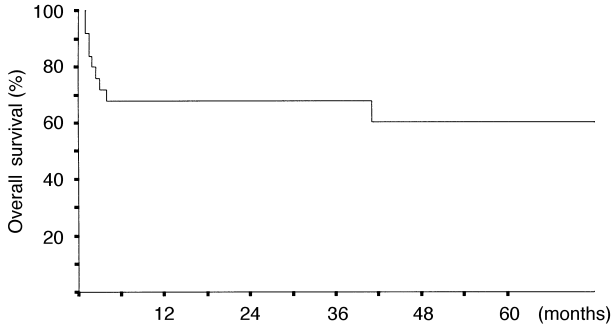

Fig. 1. Survival curve of all 25 patients from time of diagnosis.

In the absence of known malignancy, all patients with an extradural compressive lesion merit a tissue diagnosis. Spinal decompression may be preferable to biopsy alone, permitting time for a planned management approach and in our series none of the 16 patients so treated deteriorated following surgery. We cannot, however, confirm reports [21] that decompressive surgery is the major determinant of functional recovery. In common with other series we find the disease most commonly arising in the thoracic region. In the 10 years that span this report plain spinal radiology and myelography have been superseded by MRI [25]. Such studies show bony vertebral destruction is not universal, occurring in 0 to 65% of cases [3,4,9–11] emphasising the varied local mechanisms capable of producing spinal cord compression. Contrary to some reports we find no association with gender [3,9–11,16,22] nor any prognostic significance to patient age [3,9,10,12,21,22]. However, 6 of the 8 patients surviving less than 6 months from diagnosis were aged over 65 years (median 69.5 years, range: 51–78).

In common with other investigators [9,21], including those detailing SCC due to metastatic carcinoma [2,26] we found pretreatment mobility to have prognostic significance. It is reported in many series that non-ambulant patients with malignant SCC have only a 10–30% chance of becoming ambulant after therapy [1,17,27], however, earlier diagnosis and treatment are associated with improved functional outcome [2,28]. 13 patients in our series with grade 1–2 mobility improved to grades 3–4 at some point (i.e. regained independent mobility from previous paresis/paraplegia). 5 of these did so in the first week after surgery. The majority (8 patients) required between 1 and 6 months to achieve grade 3–4 mobility and clearly lack of immediate improvement after surgery does not preclude late return of function, as confirmed by others [14]. Although one previous analysis has shown sphincter dysfunction to be an independent prognostic factor [12], this is unlikely to act independent of mobility. The favourable outcome in the majority of patients reported herein supports an aggressive treatment approach, given with curative intent and aiming for maximal functional recovery.

Functional outcome may be enhanced through intensive rehabilitation in a dedicated unit [29] and we utilise an early rehabilitation programme integrating physio

and occupational therapies with medical and nursing schedules. All patients with delayed recovery are referred directly to the regional spinal injuries unit for intensive rehabilitation as soon as their condition allows.

The literature lacks a consistent approach to this condition, particularly regarding the use of dual treatment modalities [4,5,12,22]. The small number of patients herein precludes provision of dogmatic management guidelines. We suggest patients be treated along similar lines to those utilised in node-based lymphoma, based on histological type and disease stage. Given the improved control observed with the use of combined modality treatment in localised aggressive lymphomas [15,30], it is inappropriate to treat stage 1 intermediate or high-grade cases with radiation therapy alone unless other factors prevent systemic therapy. Whether chemotherapy alone is adequate for patients with localised, low volume disease is unclear, however, the low toxicity of spinal radiotherapy, the radiosensitivity of NHL and the major functional consequences of local disease recurrence favour the use of consolidation radiotherapy unless precluded by other factors. We found no patient relapsed within the CNS and would not, therefore, recommend routine CNS prophylaxis; such treatment should be restricted to those situations for which supportive evidence already exists ([31] and references therein).

Although rare, NHL should be considered in all cases of spinal cord compression thought due to malignant disease. The clinical and functional response of such patients to treatment and their more favourable overall prognosis emphasise the importance of an accurate histological diagnosis, full disease staging and the subsequent initiation of appropriate therapy.

Acknowledgement

The authors thank Mr James Paul for his assistance with statistical analysis.

References

1. Makris A, Kunkler IH. The Barthel index in assessing the response to palliative radiotherapy in malignant spinal cord compression: a prospective audit. *Clin Oncol* 1995, **7**, 82–86.
2. Maranzano E, Latini P. Effectiveness of radiation therapy without surgery in metastatic spinal cord compression: final results from a prospective trial. *Int J Radiat Oncol Biol Physics* 1995, **32**, 959–967.
3. Laing RJ, Jakubowski J, Kunkler IH, Hancock BW. Primary spinal presentation of non-Hodgkin's lymphoma: reappraisal of management and prognosis. *Spine* 1992, **17**, 117–120.
4. Epelbaum R, Haim N, Ben-Shahar M, Ben-Aire Y, Feinsod M, Cohen Y. Non-Hodgkin's lymphoma presenting with spinal epidural involvement. *Cancer* 1986, **58**, 2120–2124.
5. Di Marco A, Campostrini F, Garusi GF. Non-Hodgkin lymphomas presenting with spinal epidural involvement. *Acta Oncol* 1989, **28**, 485–488.
6. Wong ET, Portlock CS, O'Brien JP, DeAngelis LM. Chemosensitive epidural spinal cord disease in non-Hodgkin's lymphoma. *Neurology* 1996, **46**, 1543–1547.
7. Gospodarowicz MK, Sutcliffe SB, Brown TC, Chua T, Bush RS. Patterns of disease in localised extranodal lymphomas. *J Clin Oncol* 1987, **5**, 875–880.
8. Paryani S, Hoppe RT, Burke JS, *et al*. Extralymphatic involvement in diffuse non-Hodgkin's lymphoma. *J Clin Oncol* 1983, **1**, 682–688.
9. Lyons MK, O'Neill BP, Marsh WR, Kurtin PJ. Primary spinal epidural non-Hodgkin's lymphoma: report of eight patients and review of the literature. *Neurosurgery* 1992, **30**, 675–680.
10. Perry JR, Deodhare SS, Bilbao JM, Murray D, Muller P. The significance of spinal cord compression as the initial manifestation of lymphoma. *Neurosurgery* 1993, **32**, 157–162.
11. Grant JW, Kaech D, Jones DB. Spinal cord compression as the first presentation of lymphoma—a review of 15 cases. *Histopathology* 1986, **10**, 1191–1202.
12. Wallington M, Mendis S, Premawardhana U, Sanders P, Shahsavar-Haghighi K. Local control and survival in spinal cord compression from lymphoma and myeloma. *Radiother Oncol* 1997, **42**, 43–47.
13. Ron IG, Reider I, Wigler N, Chaitchik S. Primary spinal epidural non-Hodgkin's lymphoma. The contribution of nuclear magnetic resonance imaging, therapeutic approach and review of the literature. *Tumori* 1992, **78**, 397–402.
14. Tsukada T, Ohno T, Tsuji K, Kobayashi T, Deguchi K, Shirakawa S. Primary epidural non-Hodgkin's lymphoma in clinical stage IEA presenting with paraplegia and showing complete recovery after combination chemotherapy. *Inter Med* 1992, **31**, 513–515.
15. Longo DL, Glatstein E, Duffey PL, *et al*. Treatment of localised aggressive lymphomas with combination chemotherapy followed by involved field radiation therapy. *J Clin Oncol* 1989, **7**, 1295–1302.
16. Vasudev Rao T, Narayanaswamy KS, Shankar SK, Deshpande DH. Primary spinal epidural lymphomas: a clinico-pathological study. *Acta Neurochirurgica* 1982, **62**, 307–317.
17. Findlay GF. Adverse effects of the management of malignant spinal cord compression. *J Neurol Neurosurg Psychiat* 1984, **47**, 761–768.
18. Lyons MK, O'Neill BP, Kurtin PJ, Marsh WR. Diagnosis and management of primary spinal epidural non-Hodgkin's lymphoma. *Mayo Clinic Proc* 1996, **71**, 453–457.
19. Salvati M, Cervoni L, Artico M, Raco A, Ciapetta P, Delfini R. Primary spinal epidural non-Hodgkin's lymphomas: a clinical study. *Surg Neurol* 1996, **46**, 339–344.
20. Radford JA, Whelan JS, Rohatiner AZS, *et al*. Weekly VAPEC-B chemotherapy for high grade non-Hodgkin's lymphoma: results of treatment in 184 patients. *Ann Oncol* 1994, **5**, 147–151.
21. Eeles RA, O'Brien P, Horwich A, Brada M. Non-Hodgkin's lymphoma presenting with extradural spinal cord compression: functional outcome and survival. *Br J Cancer* 1991, **63**, 126–129.
22. Rathmell AJ, Gospodarowicz MK, Sutcliffe SB, Clark RM. Localised extradural lymphoma: survival, relapse pattern and functional outcome. *Radiother Oncol* 1992, **24**, 14–20.
23. Mullins GM, Flynn JPG, El-Mahdi AM, McQueen JD, Owens AH. Malignant lymphoma of the spinal epidural space. *Ann Intern Med* 1971, **74**, 416–423.
24. Haddad P, Thaell JF, Kiely JM, Harrison EG, Miller RH. Lymphoma of the spinal extradural space. *Cancer* 1976, **38**, 1862–1866.
25. Li MH, Holtas S, Larsson EM. MR imaging of spinal lymphoma. *Acta Radiol* 1992, **33**, 338–342.

26. Sorensen PS, Borgesen SE, Rohde K, *et al*. Metastatic epidural spinal cord compression: results of treatment and survival. *Cancer* 1989, **65**, 1502–1508.
27. HelwegLarsen S. Clinical outcome in metastatic spinal cord compression: a prospective study of 153 patients. *Acta Neurol Scand* 1996, **94**, 269–275.
28. Harris JK, Sutcliffe JC, Robinson NE. The role of emergency surgery in malignant spinal extradural compression: assessment of functional outcome. *Br J Neurosurg* 1996, **10**, 27–33.
29. McKinley WO. Rehabilitative functional outcome of patients with neoplastic spinal cord compression. *Arch Phys Med Rehab* 1996, **77**, 892–895.
30. Connors JM, Klimo P, Fairey RN. Brief chemotherapy and involved field radiation therapy for limited stage histologically aggressive lymphoma. *Ann Int Med* 1987, **107**, 25–29.
31. Keldsen N, Michalski W, Bentzen SM, *et al*. Risk factors for central nervous system involvement in non-Hodgkin's lymphoma. *Acta Oncol* 1996, **35**, 703–708.