Original Article

Don’t Wait for a Sensory Level – Listen to the Symptoms:
A Prospective Audit of the Delays in Diagnosis of
Malignant Cord Compression

P. Levack*, J. Graham†, D. Collie†, R. Grant†, J. Kidd‡, I. Kunkler†, A. Gibson§, D. Hurman¶, N. McMillan/*, R. Rampling||, L. Slider||, P. Statham†, D. Summers§, The Scottish Cord Compression Study Group

ABSTRACT:
Aim: To report details concerning symptoms (especially pain) preceding the development of malignant cord compression (MCC); delays between onset/reporting of symptoms and confirmed diagnosis of MCC; accuracy of investigations carried out.

Methods: A prospective observational study examined the diagnosis, management and outcome of 319 patients diagnosed with MCC at three Scottish cancer centres between January 1998–April 1999. The process was considered from the perspectives of the patient, the GP and the hospital doctor.

Results: At diagnosis, most patients (82%) were either unable to walk or only able to do so with help. Pain was reported by nearly all patients interviewed (94%) and had been present for approximately 3 months (median=90 days). It was severe in 84% of cases, with the distribution and characteristics of nerve root pain in 79%. The site of pain did not correspond to the site of compression. Where reported, weakness and/or sensory problems had been noticed by the patient for some time before diagnosis (median intervals 20 and 12 days, respectively). Most patients reported early symptoms to their General Practitioner (GP) and diagnosis was established, following referral and investigation, approximately 2 months (median=66 days) later.

Conclusion: Patients who develop spinal metastases are at risk of irreversible spinal cord damage. Weakness and sensory abnormalities are reported late and identified even later, despite patients having reported pain for a considerable time. Patients with cancer who describe severe back or spinal nerve root pain need urgent assessment on the basis of their symptoms, as signs may occur too late. Plain films and bone scans requested for patients in this audit predicted accurately the level of compression in only 21% and 19% of cases, respectively. The only accurate investigation to establish the presence and site of a compressive lesion is magnetic resonance imaging (MRI). A referral guideline based on suspicious symptoms in addition to suspicious signs is suggested. Levack, P. et al. (2002). Clinical Oncology 14, 472–480

Key words: Malignant cord compression, MRI, nerve root pain

Received: 29 October 2001 Final revised form: 27 March 2002 Accepted: 3 April 2002

Introduction
Metastatic bone disease is a common complication of cancer. When the vertebral body is involved, the resulting bone destruction may cause vertebral collapse, which in turn can cause compression of the spinal cord, cauda equina or individual nerve roots. Eventually irreversible neurological damage occurs, progressing to paraplegia. Compression may also result from a soft tissue tumour impinging directly on the spinal cord. The term malignant cord compression (MCC) applies to compression of both the spinal cord and the cauda equina.

Studies have demonstrated consistently that MCC is diagnosed late in the evolution of a compressive lesion [1–7], and that ability to walk after treatment is directly associated with ability to walk at the time of diagnosis [2,8–10]. Once this ability is lost, recovery of mobility is unlikely, and many patients subsequently need 24 h nursing care.

If outcome is to be improved, the diagnosis of MCC must be made earlier, whilst the patient is still walking. Unfortunately the most widely recognized features of cord compression (weakness, sensory loss, bowel and bladder problems) occur late in the natural history of MCC. The clinical features of early compression, which occur before walking is affected, are less widely recognized. For most patients, symptoms begin when they are...
in the community, and therefore they tend to present initially to their General Practitioner (GP). They may, or may not, be known to have cancer at presentation, and may be admitted under various hospital specialists.

The aim of this study was to assess the natural history of MCC from the onset of patient symptoms to the time of diagnosis. Specifically the study aimed to document delays in the diagnosis of MCC, to analyse their duration and where they occurred. In addition, the process of diagnosis was examined from the GP, hospital doctor and patients’ perspectives.

**Methods**

From 1 January 1998 to 14 April 1999, sequential patients diagnosed with MCC at any of three oncology centres in Scotland (The Department of Oncology, Western General Hospital, Edinburgh; The Beatson Oncology Centre, Western Infirmary, Glasgow; and Aberdeen Royal Infirmary) were recruited to the study.

The criterion for entry to the study was a definitive diagnosis of malignant cord or cauda equina compression – most often by magnetic resonance imaging (MRI) of the spine. This study did not include any patients who might have been suspected to have MCC, but were not referred for any imaging. However, in the two larger centres, we were confident that all cases of MCC diagnosed were included in the study. MCC was defined as compression, flattening or distortion of the spinal cord or cauda equina by extradural (bony or epidural) tumour, or by intradural (leptomeningeal or intraparenchymal) tumour. Patients were identified from daily review of emergency spine MRI scans, radiotherapy referral lists and referrals from clinicians involved in the management of MCC.

Approval for data collection was obtained from all relevant Primary Care and Acute Hospital NHS Trusts’ ethics committees. Individual consultants were also asked in advance for permission to interview their patients with MCC. Patients were asked whether they would be willing to participate in the interview component of the study, and written consent obtained.

**Data Entry and Analysis**

A research assistant in each centre collected and recorded all data. Data cleaning and statistical analysis were performed by the study statistician (J.K.; Information and Statistics Division, NHS, Scotland). Non-parametric data were compared using the Mann–Whitney U-test when comparing two groups and the Kruskal–Wallis test when there were three or more groups.

**Results**

**Patient Population**

Three hundred and twenty-four clinical episodes of compression were recorded in relation to 319 patients (203 male, 116 female). Eighty-nine per cent of patients were over 50 years of age at diagnosis; the median age
was 65. The commonest primary tumours were lung, prostate and breast, which together accounted for 59% of all cases. Ten per cent (32) of tumours were from the gastrointestinal tract and a further 10% were of haematological origin (myeloma, lymphoma, chronic lymphatic leukaemia). With the exception of gastrointestinal (GI) cancer, the percentage of patients seen with MCC (Fig. 1) was greater than predicted from the national cancer incidence [11], and this was most evident in prostate cancer. Although the incidence of metastatic bone disease secondary to GI cancer may be increasing, the metastatic potential for bone remains lower than the other common cancers, namely lung, prostate and breast. However with improvements in survival, morbidity related to metastatic disease from GI cancer may become more evident. In 23 cases (7%) the site of primary tumour was never identified.

Sites of Cord Compression
The level of compression was defined in terms of the vertebral body at which the uppermost part of neural compression occurred. The thoracic spine was the commonest site of MCC accounting for over two thirds of episodes in which a clear level was identified – similar to previous reports [2,7,12,13]. Thirty-five per cent occurred in the upper thoracic (T1–T6) region and 33% in the lower (T7–T12) region. Twenty-one per cent of cases occurred in the lumbar region, 7% in the cervical region, and 4% in the sacral region. Two or more concurrent compressive levels were identified in 55 out of 324 patients at imaging (17%).

Cord Compression as the First Presentation of Malignancy
Two hundred and forty-seven patients (77%) were known to have cancer before the imaging diagnosis of MCC was made. In the remaining 72 patients (23%), a diagnosis of MCC was the presenting symptom of malignancy.

Clinical Symptoms Described by Patients
Two hundred and sixty-one of 319 patients (82%) consented to be interviewed and/or for their GP to provide further information. Those patients who agreed, were interviewed a median of 3 days after they were told of their diagnosis of MCC, thus allowing the patient 48 h to consider whether or not to take part. Two hundred and forty-eight of the 261 patients who agreed to be interviewed, were able to provide a detailed personal history of their symptoms. The pattern and sequence of symptoms described by patients were very similar. Two hundred and thirty-three of 248 patients (94%) reported pain, either spinal nerve root and/or localized back pain. Seventy-nine per cent (196/248) of patients who provided a detailed history, had nerve root pain (Fig. 2), either alone in 35% (86 cases) or in association with localized back pain in 44% (110 cases). Nerve root pain was most commonly thoracic (band-like around chest or abdomen) or involving upper lumbar roots (anterior thigh pain), and was most often bilateral (66%). Fourteen per cent (35 cases) had localized back pain alone and in 1% (two cases) the nature of the pain was unclear.

Most patients (197/234; 84%) reported their pain to have been progressive, and latterly severe. The median intensity on the visual analogue pain scale was 8/10. Nearly one-third (29%) of patients assessed the severity of their pain as “the worst imagined” i.e.10/10 or even “11/10”.

Patients generally selected several words (median=3) from the list of nine characteristics, to describe their pain (Fig. 3). The most common descriptors were sharp
(59%), shooting (41%) and/or deep (36%) and the most common precipitating factors were coughing (42%), bending (40%) and/or sneezing (35%). Other qualities namely burning (30%), dull (28%) and precipitated by lying flat (19%) were less frequent. Patients often added their own adjectives, the commonest being “like toothache” (10%) and made worse by moving (14%). Pain characteristics described were similar for both lumbosacral and thoracic pain.

There was considerable discordance between the level of pain and the structural level of compression (Fig. 4). For example, more than half of patients (54%) with upper thoracic compression (T1–T6) had lumbosacral pain and conversely a similar proportion (54%) with proven lumbosacral compression had thoracic pain.

Less than one in five patients (18%) were able to walk by the time a diagnosis was made. Patients commonly reported falls, and most patients (210/248; 85%) had noticed weakness or difficulty walking beforehand. The median duration of weakness was 20 days [interquartile (IQ) range 7–132 days].

There was no association between ability to walk and the patient’s self-reported pain level as originally given on the audit form ($P=0.99$; Kruskal–Wallis test). In particular, patients who reported a pain score of 10/10 were just as likely to walk without help as those with much lower pain scores. This is illustrated (with pain scores grouped) in Fig. 5.

The majority of patients (168/248; 68%) had noticed altered sensation before the diagnosis of MCC, for a median of 12 days (IQ range 4–41 days). One hundred and thirty-nine patients (56%) reported at least one problem with passing urine, one quarter having urinary retention. Other symptoms include urinary incontinence (15%), frequency (6%), urgency (3%) and hesitancy (14%). One hundred and eighty-three (74%) of patients reported bowel problems of which by far the commonest was constipation, in 164 patients (66%). Many of these patients were on moderate or strong opioids and the constipation was commonly attributed to medication. Five per cent reported faecal incontinence.

Clinical Assessment in Hospital

In 84% of all episodes (272/324), weakness was detected on clinical examination. In 58% (87/324), sensory abnormalities were found on examination, and in 169 of these (52% of all patients), a sensory level was noted. The clinical level of sensory abnormality corresponded poorly with the level of cord compression identified on MRI imaging, varying by up to 10 dermatomes below or above the compressive lesion. In those in which a
sensory level and MRI level of compression could be compared (127 patients), the level was within three dermatomes (either above or below) in only 40% of cases. Therefore, considering the whole study population of 324 patients with MCC, a sensory level was of value in identifying the level of compression in only 16% of the MCC study group.

**Delays in Diagnosis**

We audited the chain of events and timing of them during the period from symptom onset to diagnosis. The nature of the study created some difficulties with ‘timeline’ analysis. Eighty per cent of patients in the study consented to give a detailed history, and account has to
be taken of how representative this subset was of the overall study population. Some date comparisons, for example the duration of back pain, were only relevant to those patients who had back pain. Hence the denominators changed depending on the patient subgroup being analysed, for any particular comparison between one date and another. Furthermore some dates were approximate – even though they were as accurate as the patient could remember.

The patient

Patients experienced pain (localized back and/or nerve root pain) for approximately 3 months (median=90 days; IQ range 37–205 days) before a definitive diagnosis was established and treatment given. From the point at which the patient reported their first relevant symptom to a health professional, it was approximately 2 months (median 66 days, IQ range 37–205 days; n=152;) until a compressive syndrome developed which was recognized, definitively diagnosed and documented.

Most patients interviewed (83%; 206/248), told their GP about the pain within 3 weeks (median=18 days), and at this stage 60% were already known to have a history of cancer. Patients who were already known to have cancer at the time they first developed nerve root pain (n=119), were diagnosed significantly more quickly (median 49 days) than those who were not known to have cancer (median 90 days; n=75; P<0.001, Mann–Whitney test).

Primary care

“GP referral” was defined as referral for a professional opinion to either a hospital doctor (within one of a range of specialties), a physiotherapist or other health professional. The GP referred approximately 3 weeks after the patient had first told them of their symptoms (median=18 days; IQ range 2–66 days). It was no faster for those patients known to have cancer at the time of telling their GP (P=0.32).

After referral

A diagnosis of MCC was made a median time of 15 days after referral (IQ range 3–66 days); thus in a quarter of patients for whom this time interval was calculable, the diagnosis was made 2 months or more after referral. The rate of diagnosis of MCC increased through the week and was maximal on a Friday. Few patients were diagnosed and treated at the weekends (Fig. 6), presumably reflecting the lack of access to MRI outside the working week.

Radiological Investigations

A wide range of investigations, including plain films, scintigraphy, computed tomography (CT) and MRI, were undertaken in the period from symptom onset to the time of diagnosis of MCC. Most were performed as part of the investigation of unexplained back pain, although a few were performed as part of the staging of primary malignant disease (e.g. locally advanced breast cancer), hence the inaccuracy of plain films and scintigraphy may be a slight overestimate.

Accuracy of plain films

Plain films were obtained in over half (57%) of patients before a definitive diagnosis of MCC was established; they were often arranged by the GP during the period before referral. X-rays were often of an area, which subsequently proved not to be the site of compression, but this was understandable considering that the site of pain and of compression did not correspond. The most common request was for a lumbar spine x-ray, whilst the commonest site of compression was the thoracic spine. Using the plain film sign of significant vertebral collapse (50% or more loss of vertebral height), as an indicator of MCC, plain films were highly inaccurate in predicting the level of compression. Vertebral collapse was seen in 60/187 (32%) of plain films, and in 39 of these the level of compression was confirmed on MRI. Thus in those patients who had plain films, the films obtained correctly predicted the subsequent level of compression in 21%.

Accuracy of isotope bone scintigraphy

One hundred and thirty-nine patients underwent bone scintigraphy for symptomatic back pain. Using the site of greatest activity as the most likely level of compression, bone scintigraphy was also a poor predictor of the level of compression. Forty-nine examinations had spinal hot spots suggestive of extensive bone destruction and in 26 of these, the site of greatest activity correctly predicted the level of compression, as identified on MRI. Twenty suggested an incorrect level, and three had no confirmation. Overall scintigraphy correctly predicted the level of cord compression in 26/139 (19%) examinations.
MRI

MRI was equal to or superior to all other imaging modalities at detecting cord compression. MRI detected more collapsed vertebrae than plain films, and was equivalent to bone scintigraphy in the detection of metastatic disease in adjacent and non-adjacent vertebrae.

Discussion

It is clear from our study, that at present, the majority of patients are diagnosed far too late for treatment to be of any value. Only one patient in five (18%) was able to walk without any form of help at diagnosis, and this finding was not influenced by patient age ($P=0.33$) or deprivation category ($P=0.45$). There are long delays between the onset of symptoms and diagnosis of MCC, in patients with and without a known diagnosis of malignancy.

Hence it is apparent that the current process of diagnosis is failing many patients, despite the existence of a non-invasive highly effective method of imaging (MRI). The objective should be, to alter current practice to diagnose MCC while patients are still walking. Instead of making a diagnosis of MCC, which is beyond all suspicion, i.e. based on ‘hard’ clinical signs, the patient who has malignant epidural disease, and other patients at high risk of developing MCC, need to be identified earlier.

Although a lot of emphasis is put on clinical signs of MCC, in practice they are often identified late, if at all. Problems with walking are often attributed to pain, but as can be seen from the data presented here, patients reporting their pain to be 10/10 were just as likely to be able to walk as those whose pain was much less. A sensory level was noted in half the patients (52%) but by the time it was noted, the majority of these patients were unable to walk and therefore the presence of a sensory level does not help in detecting MCC before motor loss.

There is a lack of awareness in both primary and secondary care of the early symptoms of MCC. Symptoms in the cancer population have a different significance to symptoms in the general, non-cancer population. Progressive and severe pain in cancer patients is usually related to cancer progression or recurrence, and a recent study indicated that 92% of severe pain in cancer patients was due to tumour involvement [14]. In our study, severe nerve root pain was strongly associated with epidural disease and was reported by patients long before weakness.

Furthermore in this study, patients’ descriptions of pain – its severity and its characteristics – were remarkably consistent. Using a checklist of cancer pain syndromes previously described [15], the Task Force on Cancer Pain of the International Association for the Study of Pain [14] identified 22 cancer pain syndromes and the pain attributed to neural involvement was often described as amongst the most intense. Although Bayley et al. in a recent publication [16] did not find the presence or absence of pain, or the use of opioid analgesia to be an independent prognostic factor for occult MCC, in patients with known metastatic bone disease they did not define the nature of pain, the presence or absence of nerve root pain or the means by which a pain history was taken.

The diagnostic value of the words patients use to describe their pain has been examined by several authors [12,17,18], mainly to differentiate nerve root pain from non-nerve root pain. Such studies usually included patients with a mixture of malignant and non-malignant conditions. In our study, in which most patients had MRI-proven confirmation of malignant compression of the spinal cord, pain was most commonly described as sharp and precipitated by coughing or bending, irrespective of whether the pain was thoracic or lumbosacral. Lying flat was the least frequently reported quality. Our study found that severe nerve root pain was strongly associated with root and cord compression, and this pain syndrome can be recognized by making a careful pain assessment including its distribution, severity, the words used to describe it and the factors that provoke it.

With regard to investigations, this study has shown that there is a lack of awareness and/or access, to the most useful investigation of back pain in malignancy. We have shown that plain films are an insensitive method of detecting bone metastases compared to MRI, particularly in tumours not causing cortical bone destruction, and bone scintigraphy is insensitive to the presence of neural compression. Yet much time was spent by hospital doctors and GPs, arranging plain films and bone scintigraphy, which, in many cases added little to establishing a diagnosis of root or cord compression. Indeed it is highly likely that initial investigation with plain films and/or bone scintigraphy contributed to delays in diagnosis in some cases.

The specific issues the clinician wishes to answer by radiological investigation, are (1) whether there is tumour compressing the cord or a nerve; (2) whether the spine is stable and (3) what treatment should be used and on what site. These questions can only be answered satisfactorily with MRI. The existence and the quality of the pain appear more important than the site of pain, as the latter correlated poorly with site of compression. Neither the site of pain, nor the location of a sensory level, (if any) is reliable enough to establish the diagnosis of MCC or select the level of radiological assessment. Therefore MRI of the whole spine is the only suitable investigation, in patients with severe back or nerve root pain and known malignancy. Other investigations probably delay diagnosis because of waiting times and the false reassurance they can give to the patient’s clinician.

Unfortunately MRI is not available in many hospitals out of hours, and the low percentage of patients in whom MCC was confirmed by MRI at the weekends, contributes to the delay in diagnosis and management. MRI is often difficult even to arrange during normal
Emergency referral (suspected malignant cord compression)

\[
\text{cancer or} \quad + \quad \text{myelopathy} \quad \rightarrow \quad \text{ADMIT}
\]

\[
\text{suspected cancer} \quad \text{(i.e. weakness, sensory loss, urinary retention)}
\]

Urgent referral (suspected malignant epidural disease)

\[
\text{cancer} \quad + \quad \text{suspicious pain} \quad \rightarrow \quad \text{URGENT MRI}
\]

which cancers are most at risk?

- breast & prostate & lung but a complication of most cancers
- known bone metastases

which pain is suspicious?

- nerve root pain – often described as tingling, burning, shooting, especially anterior thigh, around chest wall and posterior thigh
- localised back pain - especially thoracic
- severe, progressive pain, poorly responsive to medicines

Fig. 7 – Proposed referral guideline.

working hours, as patients are selected on the basis of having “clear evidence of compression”. Those patients without significant weakness, and often those without a sensory level, may fail to qualify. Despite widespread awareness of the need to diagnose MCC early, the very justification for MRI often depends on clinical findings, which occur late.

This study also highlights the problem of “parallel care” of patients who, following referral, remain in the primary care environment but are also in the hospital out-patient system. It was clear from listening to patients, that whilst investigations were pending, symptoms often deteriorated. After making the referral, the GP was not always able to influence arrangements and timing of planned investigations. Despite the recognized importance of early diagnosis, there frequently appeared to be little sense of urgency.

Certain categories of patients are at risk of MCC, specifically patients who are already known to have cancer when they first develop pain, who are over the age of 50, and those with breast or prostate cancer with known bone metastases. Prostate and breast cancer is widely recognized to metastasise readily to bone and a recent study has demonstrated the high incidence of occult epidural disease and MCC, in patients with prostate cancer, in whom neurological examination was normal. [16]. The likelihood of occult epidural disease was highest in those patients with hormone refractory disease, and extensive (>20) bone metastases detected on bone scan.

MCC is a clinical emergency and delays in diagnosis and treatment have devastating consequences for patients and their families. Consequently GPs are frequently exhorted to refer patients with cord compression early, whilst at the same time being discouraged from over-referring patients who have “uncomplicated” back pain. The Royal College of General Practitioners “Guidelines for the management of acute low back pain” [19] alert the practitioner to specific symptoms and signs, which may indicate serious disorders. However the guideline is intended for the general population, in which acute low back pain due to degenerative disease is common. It differentiates back pain into three separate categories: simple mechanical backache, nerve root (leg) pain and possible serious spinal problem. There are no guidelines specifically for patients already known to have cancer and who develop back pain, and it is clear from our findings that nerve root (leg) pain and a serious spinal problem (MCC) frequently co-exist.

This study confirms that despite a long history of painful symptoms and a past diagnosis of cancer, the diagnosis of MCC is still being made late. Therefore, in order to:

1) Reduce delays in diagnosis and referral, the authors propose a national programme of awareness of MCC, in order to highlight in particular the association of severe nerve root pain with epidural disease, in patients with cancer. The ability to distinguish nerve root pain from non-nerve root
pain needs to be considerably improved. Patients in our study did not delay long before seeking help, but it may be appropriate for patients to be educated as above.

(2) Ensure an efficient and accessible referral process is in place, referral guidelines are currently being developed to urgently image with MRI patients who are “at risk of having epidural disease or evolving compression” as shown in Fig. 7. This process however, will almost certainly depend on increased MRI availability.

Acknowledgements. This study was funded by a grant from CRAG Clinical Research and Audit group of the Scottish Office, and the report was submitted in July 2001. The Scottish Health Executive has subsequently agreed to implement the report’s findings.

References