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Occasional review

Adverse effects of the management of malignant spinal cord compression

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SUMMARY As a prelude to further work which attempts to improve the management of metastatic spinal cord compression the efficacy and adverse effects of existing therapy has been assessed. All papers dealing with the management of malignant spinal cord compression since 1960 have been reviewed. Data from this review is presented in a novel manner in order to identify not only the degree of successful return to ambulation achieved but more importantly the extent of the adverse effects which occur during existing management. It is seen that, while in general some 35% of patients treated in any manner retain or return to the ability to walk, some 20% to 25% sustain major neurological deterioration. In addition, those patients treated by laminectomy who do deteriorate may be subject to a significant rate of perioperative mortality and major structural complications related to the surgical wounds. In the light of the adverse factors described, the role of laminectomy as first-line management of malignant cord compression is questioned. Alternative modes of treatment are discussed and a tentative scheme of management described which it is hoped will lead to a better quality of survival of the group as a whole in addition to maintaining, or perhaps, improving the rate of successful return to ambulation.

The management of metastases arising in the spinal column which cause neurological deficit has caused debate for many years. The traditional method of treatment is of immediate surgical decompression by laminectomy followed in some or all cases by radiotherapy. More recently attention has been given to primary radiotherapy as the treatment of first choice.[1–5] Some attempts[1–6] have been made to compare these management methods but the absence of a satisfactory, controlled trial still leaves no clear concensus on management. Previous papers have concentrated, understandably, on the efficacy of the techniques under consideration. Whilst adverse effects have been noted in passing, little attention has been given to the complications of therapy. In a disease with a severely limited life span such as metastatic cord compression, whilst successful return to ambulation remains the goal, the quality of survival of the whole group attains paramount importance.

This review has been made in an attempt to achieve an objective picture of the effects of existing management of spinal cord compression. Data has been extracted in order to assess in practical, functional terms not only the benefits but also the costs of such treatment. The data is used as a basis for suggesting a scheme of management designed to produce maximum recovery with minimal adverse effects.

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Methods

All papers concerning malignant spinal cord compression published since 1960 have been reviewed. No attempt has been made to compare individual series; rather, data has been extracted wherever possible from papers and used to construct overall tables concerning different types of therapy. Regrettably, many of the series either described their cases in insufficient detail to allow analysis or used inexact terms such as "improvement" or "success" without

Table 1 *Results when ambulant on presentation*

Mode of therapy	*No of cases*	*% Good histology*	*% Still ambulant following treatment*	*% Neurologically worse following treatment*
Laminectomy alone	81	17%	48%	52%
Laminectomy ± radiotherapy*	240	28%	67%	33%
Radiotherapy alone	126	25%	79%	21%

*Laminectomy with appropriate radiotherapy.

adequate definition. Such papers were not considered further, and only those series presenting data in such a way as to allow analysis as described below were included.[1-5 7-23]

A total of 1816 cases were identified about which data were accurately available for inclusion in this paper. In some of these cases information was provided only on certain aspects considered in this review; accordingly the numbers included in each table varies as to the available data. The treatments used in the various studies were of standard type, falling into three groups. The first group included patients treated by laminectomy alone without recourse to radiotherapy. The next group included patients from series where treatment was by immediate laminectomy supported by follow up radiotherapy where appropriate. In this group the indications for radiotherapy varied but approximately 50% of the patients underwent radiation treatment following the laminectomy. The final group consisted of patients who did not undergo surgery but were treated by urgent radiotherapy, usually with steroids. For purposes of comparison a further group of patients treated by anterior surgical approach to the spine is included in the discussion section.

Major emphasis was placed on being able to identify accurately the neurological status of patients on presentation. Confirmation that this dramatically effects outcome has been shown again recently by Constans *et al.*[11] Data was collected solely from series where it was possible to classify patients according to one of the following groups: ambulant—with or without a walking aid; paraparetic but non-ambulant; and complete motor and sensory paraplegia. Sphincteric disturbance was not studied. With regard to the outcome of therapy, papers reporting only in terms such as "neurological improvement" were disregarded. Only those series where the neurological status following therapy could be identified and classified into the grades given above were included. Movement to a better grade following treatment was the sole criterion accepted as showing success of that treatment. Equally, change to a worse grade was accepted as deterioration. The timing of the evaluation of such therapy varied between series, but usually was made within the first month. Any deterioration occurring along with the terminal stages of the disease process was disregarded by all authors.

Mortality rates and the frequency of occurrence of certain non-neurological complications of therapy were also studied. Mortality rates were taken as deaths occurring within one month of therapy. Complications such as chest infection and pulmonary embolus were excluded from all groups. The only non-neurological complications of surgical therapy considered were those directly associated with operation, namely: wound infection or dehiscence; and spinal instability.

The histological makeup of each series was examined. An attempt was made to extrapolate to the tables presented in this communication an approximation of the proportion of patients in each group with tumours of favourable histology. Favourable tumours were taken as lymphoreticular and prostatic tumours, and myeloma. Papers which presented data exclusively on lymphoreticular tumours were excluded.

The achievement or otherwise of pain relief was also examined. Each of the authors reported pain and its relief in a purely subjective manner. Accordingly reliance had to be placed on the individual authors' assessment of satisfactory pain relief.

Results

Neurological Outcome

Table 1 presents the results of treating patients who remain able to walk—even with an aid—at presentation. The histological make up of each group is comparable. It can be seen that, following treatment, the number who were still able to walk had dropped to between 48% and 79% of those presenting. Thus, between 21% and 52% of these patients had become non-ambulant and therefore suffered not only major deterioration but failure of treatment. The fact that only 447 patients could be collected for this table from this extensive review shows that only 25% of the total 1816 patients presented while still being able to walk.

The results of treating patients who are paraparetic but non-ambulant are presented in table 2. The

Table 2 *Results when paraparetic on presentation*

Mode of therapy	*No of cases*	*% Good histology*	*% Becoming ambulant following treatment*	*% Neurologically worse following treatment*
Laminectomy alone	134	19%	31%	32%
Laminectomy ± radiotherapy	419	27%	35%	17%
Radiotherapy alone	144	20%	42%	22%

Table 3 *Results when paraplegic on presentation*

Mode of therapy	*No of cases*	*% Good histology*	*% Becoming ambulant following treatment**
Laminectomy alone	40	17%	3%
Laminectomy ± radiotherapy	163	26%	7%
Radiotherapy alone	45	20%	2%

*Neurological deterioration not applicable.

group of patients undergoing laminectomy with appropriate radiotherapy contains a greater number of cases of favourable histology than do the other groups. The table shows that the number of patients who regained the ability to walk ranged from 31% to 42%. Also shown are the number of patients who deteriorated to the paraplegic group following therapy and this varied from 17% to 32%.

Table 3 presents the results in similar manner for patients who were paraplegic on presentation. As functional recovery was deemed to be the prime goal of therapy only those patients recovering the ability to walk are shown. As these patients were paraplegic already, neurological deterioration could obviously not occur.

Several papers did not present data in sufficient detail to be included in the above analysis. However, some of these series gave sufficiently accurate overall results to identify the number of patients who were ambulant on presentation and those that were ambulant following treatment. By including these patients an overall estimate of the effects of treatment can be derived and this is presented in table 4. It was possible to determine the number of patients who suffered neurological deterioration by extrapolation.

As has been shown, major neurological deterioration occurred in many patients. Table 5 summarises the occurrence of such neurological deterioration. The number of patients experiencing deterioration of at least one functional grade is shown for those patients who were either ambulant or paraparetic on presentation. The number showing deterioration in the overall groups is also presented.

Mortality

Most papers dealing with surgical therapy reported mortality rates. Different authors determined this at either two weeks or one month from surgery. Only two of the papers[7 19] which dealt with laminectomy alone reported mortality rates which were 16% and 24%. In the group treated by laminectomy with appropriate radiotherapy, the mortality rate ranged between 6% and 12% with a mean of 9% reported cases. Therapy mortality rates were not reported in any of the radiotherapy series.

Non-neurological complications

The series using laminectomy as sole treatment did not report on complications.

In the group treated by laminectomy with appropriate radiotherapy, series comprising 391 patients reported on non-neurological complications. Of these patients, 11% developed a complication; these being either wound infection, dehiscence or spinal instability. With regard to the problem of instability, only two authors[2 20] specifically mention instability. Of the 65 cases, on which they reported, six (9%) developed post-laminectomy spinal instability.

Papers reporting on radiotherapy alone did not mention complication rates.

Pain relief

Many authors reported on pain relief. Their assessments are presented on table 6. The percentages

Table 4 *Overall results*

Mode of therapy	*No of cases*	*% Good histology*	*% Ambulant on presentation*	*% Ambulant following treatment*	*% Neurologically worse following treatment*
Laminectomy alone	261	17%	34%	32%	26%
Laminectomy ± radiotherapy	1240	28%	31%	38%	20%
Radiotherapy alone	315	20%	44%	51%	17%

Table 5 *Neurological deterioration following treatment*

Mode of therapy	*% Undergoing neurological deterioration following treatment*		
	Ambulant on presentation	*Paretic on presentation*	*Overall cases*
Laminectomy alone	52%	32%	26%
Laminectomy ± radiotherapy	33%	17%	20%
Radiotherapy alone	21%	22%	17%

Table 6 *Pain relief*

Mode of therapy	*No of cases*	*% Good histology*	*Pain relief achieved*
Laminectomy alone	190	16%	36%
Laminectomy ± radiotherapy	141	25%	67%
Radiotherapy alone	114	19%	76%

therein refer to the number of patients who experienced pain at the time of presentation but who achieved adequate relief following treatment. No series commented on either patients who developed or had their pain increased following treatment.

Discussion

Previous reports concerning the management of malignant spinal cord compression have concentrated on the efficacy of the treatment involved. Scant attention has been paid to the complications and deleterious affects of such treatment. The management of such a problem as malignant cord compression can never be curative in its own right. This simple fact emphasises the importance of considering not only the success of treatment but also the effect of that treatment on the quality of further survival of the entire group.

Many of these previous papers have expressed results in imprecise terms, relying on terms such as "improved". The only truly acceptable outcomes for therapy of this disease are return to ambulation, sphincter recovery and pain relief. This study has looked primarily at neurological function. The inclusion of only those papers in which sufficiently precise data was presented has allowed cases to be categorised into one of three easily defined neurological groups both prior to and following therapy. Success or failure of therapy was judged solely by transference of patients between categories. This further reflects the importance of major functional improvement as being the only truly successful outcome. Minor, non-functional improvement is insufficient to improve the quality of survival and therefore patients credited with success are those who showed only major improvement by at least one grade. Equally those patients judged to have deteriorated by this method have experienced a major, functional loss.

Previous reviews[6] on the subject have attempted to compare the results of widely differing series, frequently of varying histological make up and consisting of different numbers of patients presenting while still ambulant. It is not surprising perhaps that no clear difference emerges between the various therapies used. This study has attempted to avoid this problem by extracting information from various papers to collate new tables of data rather than comparing studies. This approach also has limitations; and accordingly, no attempt has been made to decide which treatment is better or worse. Rather, an attempt has been made to highlight the general expectation of successful outcome and, more importantly, the chances of making patients worse.

With regard to successful neurological outcome, this paper shows that overall in 1816 patients only 32%, 38% and 51% of patients treated by laminectomy alone, laminectomy with appropriate radiotherapy, or radiotherapy alone, respectively, were able to walk at the end of their treatment. Owing to the limitations expressed above it is wrong to conclude from this data that radiotherapy is a better treatment, as for instance, the radiotherapy group had a greater number of people ambulant on presentation. It is reasonable to conclude, however, that no gross difference exists in efficacy. In addition the number who deteriorated by a full grade following therapy was similar for each therapy, being 26%, 20% and 17% respectively.

When only those patients identifiable as being ambulant on presentation are considered the percentage who can still walk following treatment is much more satisfactory, ranging from 48% to 79%. However, this means that between one fifth and one half of the patients have lost the power to walk shortly after treatment and, therefore, treatment has failed. When considering patients who are paraparetic but non-ambulant on presenation, it is seen that whilst approximately one third can walk again, one quarter have become paraplegic. It is not surprising that the number of people paraplegic on admission who walk again is small. Obviously these patients cannot suffer further neurological deterioration.

The frequency with which neurological deterioration severe enough to cause a change of grading occurs is considerable. If one considers only those patients treated by primary radiotherapy or by laminectomy with appropriate radiotherapy, approximately 25% of those ambulant on presentation will deteriorate. Similarly, of those paraparetic before therapy some 20% will get worse.

With regard to pain relief, it seems that laminectomy alone gives poor results. There seems to be little to choose between the other treatments with regard to pain relief. No authors comment on patients who either develop pain or have an exacerbation of pain following therapy, although clinical experience does show that this happens.

The papers dealing with radiotherapy alone do not comment on mortality or complications of therapy. It seems reasonable to assume, however, that death in the first month following radiotherapy is likely to be due to the primary disease. The two

early papers reporting mortality rates of 16% and 24% for surgery alone probably do not reflect modern experience. With regard to the laminectomy with appropriate radiotherapy group, 9% of these patients died within one month of surgery. Although some of these deaths might be due to primary disease, all authors were careful to point out that unfit or end-stage patients were excluded.

In addition to the neurological complications described above, wound-related complications were prominent in the surgical group. Only a relatively few authors describe these complications but in those who did so the rate was 11%. More disturbing is the fact that from the two papers specifically discussing postoperative spinal instability, 9% of their cases showed evidence of this particular devastating complication.

From these papers it is difficult to determine which factor might predispose to a bad neurological outcome or to surgical complications. It proved impossible to determine from the data available whether the speed of onset or length of history had any effect on this. However, there seem to be equal numbers of authors concluding that these factors were or were not important. With regard to vertebral collapse, some authors stated that collapse reduced the chances of neurological recovery but gave only scant data to support their statements. It was possible to identify only 47 patients (all treated with laminectomy and appropriate radiotherapy) with vertebral collapse of whom only 21% were ambulant following therapy. This is considerably less than the overall figure of 38% ambulant following such therapy. In addition Brice and McKissock[9] stated that in their study, which included 30 patients with collapse "no patient with severe neurological deficit and vertebral collapse improved" with laminectomy and radiotherapy.

The one factor which does appear to affect prognosis is the ability still to walk at the time of presentation. Approximately twice the number presenting in this state were able to walk following treatment as compared to the paraparetic group. Nevertheless approximately one third of these patients deteriorated so that they could not walk following therapy. It seems clear, however, that the quality of life of patients with malignant cord compression as a whole could be improved dramatically by early diagnosis and treatment. It is depressing to note that only one quarter of the patients in this extensive review presented while still being able to walk.

The present situation appears to be that accepted standard treatment leads only to limited success. Almost as many patients deteriorate shortly after treatment as those who improve and return to being able to walk. In addition, laminectomy carries a considerable risk of mortality and non-neurological wound complication which can leave the patient much worse off than prior to therapy.

Laminectomy has been advocated in the past as a means to achieve tissue diagnosis. Treatment can not be effectively planned in the absence of a definitive diagnosis and so alternative methods would have to be used for diagnosis if laminectomy were to be avoided. This can be easily and effectively achieved in the presence of vertebral collapse by percutaneous needle biopsy.[24] If collapse is not present, a tissue diagnosis can be obtained by a small posterior approach with hemilaminectomy if tumour is not actually found in the paravertebral muscle or bone.

The adverse results of existing therapy have lead some surgeons to attempt an alternative approach to the spine by way of an anterolateral route. Several cases of such surgery have been reported recently,[25–30] though no large study exists. These are all obviously highly selected patients and therefore should not be compared too closely to the other groups. Nevertheless, the results of anterior surgery as reported are presented in table 7. These dramatic results certainly suggest that major neurological recovery is possible by this technique although it is unclear as to how often such success could be achieved.

The adverse effects of existing treatment have been high-lighted in this review. The results of primary radiotherapy seem comparable in terms of both efficacy and adversity to those of urgent laminectomy with appropriate radiotherapy. Laminectomy on its own, however, seems to produce much worse results. The data presented in this review must lead one to question whether it is the

Table 7 *Results of anterior spinal surgery*

Pre-operative neurological state	*No of cases*	*% Good histology*	*% Ambulant following treatment*	*% Neurologically worse following treatment*
Ambulant	18	28%	94%	6%
Paretic	11	20%	82%	0%
Plegic	7	20%	43%	N/A †
Overall*	51	21%	84%	8%

*Includes a further 15 cases of undetermined neurological state.
†Not appropriate.

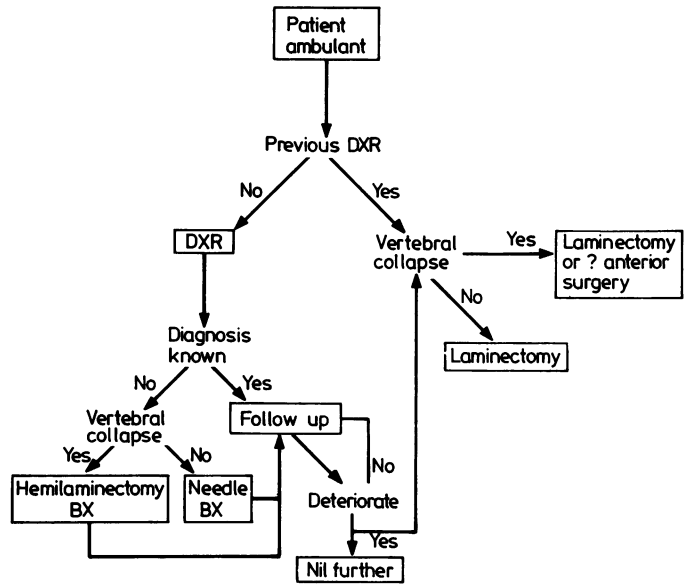

Fig 1 *Suggested management scheme for patients presenting while still ambulant.*

"appropriate radiotherapy" following laminectomy which brings this group to such a comparable position. The limited success rate of laminectomy is balanced by almost equal rate of adverse neurological effects. When combined with the other non-neurological complications and mortality, the role of laminectomy as the first-line therapy for malignant spinal cord compression must be questioned. There is little doubt that radiotherapy supported by steroids can give comparable results. Undoubtedly, patients treated by radiotherapy can deteriorate neurologically in the same way as surgical patients but they are spared the other adverse effects of surgery. Those who do deteriorate following radiotherapy could still undergo laminectomy as a treatment option at an early stage in their deterioration.

There have been fears that urgent radiotherapy without bony decompression could have deleterious effects. This paper shows that this does not happen any more often than occurs following decompression alone. Additionally, Rubin[31] has shown that, provided adequate initial radiotherapeutic doses are used along with steroids, tumour shrinkage does occur immediately without swelling. These factors suggest that treatment by radiotherapy with steroids in the first instance will give comparable results in terms of success but with less of the remainder suffering deterioration in their quality of survival.

There is a suggestion from some of the papers reviewed that vertebral collapse increases the risk of laminectomy. The presence of collapse must increase the risk of post-laminectomy instability. A study is in progress in this department to evaluate the role of vertebral collapse on outcome. It seems possible that, in patients with collapse, primary radiotherapy with steroids could lead to better results and almost certainly to lesser morbidity.

In the face of such adverse effects as have been made evident in this review, laminectomy cannot be justified either as a means of obtaining tissue diagnosis or as a first line treatment in all cases. Laminectomy as a decompressive procedure probably should be reserved for patients without vertebral collapse who have either had previous radiotherapy or who deteriorate during their initial radiotherapy treatment.

Based on the assumptions drawn from this review, potential schemes of management are presented. Figure 1 represents a suggested scheme for the management of patients presenting whilst still ambulant with the primary therapy being radiation if possible. Patients who present after becoming non-ambulant but who do not have vertebral collapse would also be managed along these lines. Figure 2 presents a scheme of management for non-ambulant patients who do have collapse of a vertebral body. Laminectomy is avoided in these patients. These schemes are designed not only to improve the rate of successful return to ambulation in patients with malignant cord

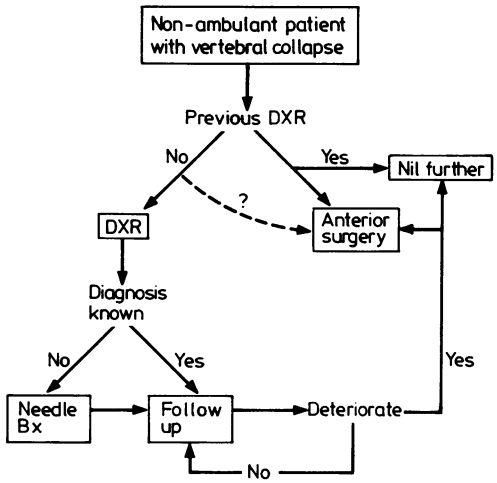

Fig 2 *Suggested management scheme for non-ambulant patients.*

compression but also to minimise the adverse effects of therapy on the group as a whole. Whether these aims can be achieved remains to be proven.

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