Surgical Treatment of Malignant Extradural Spinal Tumours

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In these days of increasing control of malignant neoplastic disease the treatment of apparently single metastases or of inoperable but strategically situated neoplasms assumes a greater importance. There are few situations in the body where a relatively small neoplasm may cause such a major disturbance to the individual as in the spinal extradural space. This space with its rich supply of blood-vessels and lymphatics forms a common site for the implantation of metastatic deposits. It may be invaded by malignant disease from associated structures and occasionally primary neoplasms appear to arise from tissues within the space. In the past the treatment of these conditions has appeared unsatisfactory (Shenkin *et al.*, 1945) if assessed in terms of cure or survival time. Since cure is unlikely it seemed worth while to revise and study this problem, particularly with regard to the symptomatic relief obtained using surgery supplemented by other forms of therapy.

Accordingly the clinical records of 160 patients seen in the last 10 years, in whom a definite diagnosis of malignant disease in the spinal extradural space was made, have been examined. As most of these patients present a similar clinical problem—that of paraparesis of unknown origin—all types of malignant disease have been included, though some of the case material has been presented elsewhere (Bhagwati and McKissock, 1961 ; McKissock *et al.*, 1961).

Table I shows the range and incidence of the clinical material. Clearly this cannot be a true spectrum of malignant tumours in the extradural space. Comparison with other large series (Törma, 1957 ; Arseni *et al.*, 1959 ; Botterell and Fitzgerald, 1959 ; Kennady and Stern, 1962) shows a different incidence of various types of disease. Selection of material on the part of the referring physicians and surgeons has taken place before the patients enter a neurosurgical centre. Other clinical specialties, such as radiotherapy and general surgery, are concerned in the management of this type of disease, and those conditions in which there are other effective means of treatment available or in which metastases appear late may not reach the neurosurgeon. Comparison of results is therefore difficult if not impossible. Despite the selection it is possible in a reasonably large series to seek diagnostic and prognostic factors which may improve an otherwise gloomy outlook. With this in mind the records of 145 patients have been examined. An additional 15 patients were seen during the 10-year period, in nine of whom the disease was too far advanced to warrant surgical intervention, while the remaining six patients showed predominantly root lesions. These two small groups have been discarded, as no conclusions can be drawn from them.

TABLE I.—*Malignant Extradural Spinal Tumours: Pathological Types and Results Achieved*

Pathology	No.	Satisfactory Results	Survivors 1–10 yr.
Metastatic carcinoma			
1. Bronchus	28	2	0
2. Breast	12	7	3
3. Prostate	8	3	1
4. Kidney	3	0	0
5. Colon	2	0	0
6. Oesophagus	1	0	0
7. Bladder	1	0	0
8. Unknown	38	7	2
Other metastases			
1. Sarcoma	4	1	0
2. Melanoma	1	0	0
3. Teratoma	1	1	0
Total metastases	99	21	6
"Reticuloses"			
1. Myeloma	30	16	9
2. Lymphadenoma	9	6	3
Primary sarcomas	7	1	1
Totals	145	44	19

Clinical Picture

As others have commented (Botterell and Fitzgerald, 1959) the striking feature of the clinical presentation of these patients is their similarity. There can be few diseases which present such a uniform pattern. Despite variations in site and pathology the history in 90% of patients was that of pain in the back localized to the area involved, often associated with root pains in the local neurological segments. In the trunk these pains were often of girdle type, though when the cervical or upper lumbar segments were involved unilateral pain was a more common feature. The fact that these symptoms of nerve-root compression were often accentuated by straining, coughing, or sneezing gave rise to early diagnostic difficulties when the complaints were attributed to mechanical disorders of the spine, such as osteoarthritis or intervertebral disk disease. These symptoms were then followed after a variable period of time by the onset of spinal-cord compression. The rate at which this appeared varied considerably : in some patients it was abrupt, in others spread over many weeks. This speed of onset of spinal-cord involvement was found to have considerable bearing on the ultimate prognosis.

Again, despite variation in rate of onset the clinical pattern of developing spinal-cord compression was remarkably constant. Thus, in a slow and complete progression the patient would notice motor weakness of the legs followed by sensory loss. Loss of sphincter control occurred later and the last vestige of cord function disappeared with the loss of appreciation of deep pain below the already established sensory level. These observations support those of Tarlov (1957) in clinical and experimental studies, and suggest that major neuronal tracts in the spinal cord possess a selective sensitivity to compression. For this reason it is not possible to forecast clinically the relationship of the tumour mass to various aspects of the cord, though lateralization can be predicted from the involvement of one leg before another. A lateral cord syndrome (Brown-Séquard) was seen only rarely in this series, unlike those of intradural compression (Kinnear Wilson, 1955). All patients showed varying degrees of neurological deficit attributable to spinal-cord compression. These deficits were divided for convenience into four groups (Table II) : (1) mild—able to walk ; (2) Moderate—able to move legs but not against gravity ; (3) Severe—slight residual motor and sensory function, with retention of deep pain sensation ; (4) Complete—no signs of motor, sensory, or normal

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sphincter function below lesion in cord. This clinical classification proved useful for prognostic purposes.

TABLE II.—*Results Classified According to Clinical State of Patient*

Severity of Neurological Lesion	No.	Satisfactory Results	% Success
Mild	16	11	70
Moderate	36	15	45
Severe	55	18	33
Complete	38	0	0
Total	145	44	—

Differential diagnosis from other causes of acute paraplegia was not usually difficult. Occasionally conditions such as spinal extradural abscess, extradural haematoma, tuberculosis without obvious bony changes, Paget's disease, and benign extradural tumours caused difficulties. Surgical intervention usually clarified the position, a point of considerable importance when the treatment of urgent conditions such as an extradural abscess arose. Differentiation within the group of conditions under consideration was much more difficult.

Clinical evidence of disease elsewhere was seen in only 19 instances but a history of neoplastic disease was obtained in 23 cases. Again selection before referral obviously played a part. In most patients there was little to suggest malignant disease, and in many cases a diligent search at a later date failed to reveal the site of the primary lesion. In under one-half of the patients with histologically verified metastatic disease (Table I) this site was not identified during life. Clearly in many patients it is futile and a waste of valuable time to indulge in a prolonged search in the face of advancing spinal-cord compression. Several patients in this series suffered irreparable damage to the spinal cord while unsuccessful attempts at a precise pathological diagnosis were being made by referring clinicians.

Investigations

In general haematological investigations were not helpful. Many patients showed an elevated erythrocytic sedimentation rate, but as urinary infections and occasional pressure sores were present the significance of this result was doubtful. In the group of myeloma cases few showed any disturbance of serum proteins, and the results were often not available before a definite pathological diagnosis had been established.

Lumbar puncture often revealed evidence of a block, and the protein level in the fluid was almost invariably raised, within the range of 70–3,000 mg./100 ml. This protein level seemed unrelated to the site or cause of the block. The examination itself is not without risk in these patients, as on two occasions a complete spinal-cord lesion developed shortly after a lumbar puncture. Törma (1957) noted 16 instances in a series of 201 patients in which paralysis developed within two days of a lumbar puncture having been performed. Difficulties may also arise at subsequent myelography, and for these reasons the procedure is better reserved for the performance of myelography shortly before surgical treatment is carried out.

The more significant investigations were radiological. In plain radiographs of the appropriate areas the findings in order of frequency were loss of one or more pedicles, partial collapse of a vertebral body, or a paravertebral soft tissue mass; occasionally erosion of a lamina or deposits in the spinous processes could be seen. Loss of definition of a vertebral pedicle was the earliest change noted. With involvement of the cervical spine gross changes in the bones could be seen before marked spinal-cord involvement developed, presumably owing to the greater width of the cervical canal. Ten per cent. of patients showed no obvious changes in plain radiographs of the appropriate area. Plain radiography of the chest and other parts of the skeletal system occasionally enabled the radiologist to predict the histological diagnosis, but it is significant that if such simple investigations failed to show a primary source of the disease other more elaborate methods rarely helped the clinician.

Almost all patients were found to have some degree of spinal block on myelography, usually complete. Though the common abnormality seen was an irregular termination of the Myodil column with displacement of that column away from the pedicle or vertebral body, it was possible from displacement of the cord shadow to predict the likely relationship of the main tumour mass to the spinal theca. Thus the radiologist could forecast a predominantly anterior, lateral, or posterior compression, and these predictions correlated reasonably well with the operative findings.

Operative Findings

All but nine patients were subjected to laminectomy, first to establish the diagnosis beyond all doubt and second to carry out an adequate rapid decompression of the spinal cord before other appropriate therapeutic measures were undertaken. The findings were those of irregular masses of obviously malignant tissue situated in the extradural space, occasionally continuous with further tumour tissue within the vertebral body or paraspinal masses in the erector spinae muscles or posterior mediastinum. This tissue was adherent to the dura but in only two cases had it actually penetrated this membrane. The configuration of these masses could be divided broadly into four groups: (1) Irregular multiple masses not apparently connected together; (2) a cuff of tissue concentrically constricting the spinal theca; (3) a diffuse plaque applied to one aspect of the theca; (4) a localized circumscribed mass.

Only in the last group could anything approaching a complete macroscopical removal be achieved.

Post-operative Complications

In the immediate post-operative period many patients developed urinary and chest infections, but these were adequately controlled with antibiotic or sulphonamide therapy. As many patients were received with early infections it was not possible to assess the relationship of operation to these complications. Other more obvious post-operative complications occurred. Two patients developed a severe intractable paralytic ileus from which they died. In another three patients with high thoracic disease wound dehiscence occurred requiring resuture. Ten patients deteriorated neurologically, and it is of interest that seven of these patients suffered anterior compression of the thoracic spinal cord, the neurological deterioration occurring on the second or third day after operation. Similar deterioration may occur after laminectomy for a prolapsed thoracic intervertebral disk or other types of anterior compression. Perhaps another approach, such as an antero-lateral one, would be more successful in this type of compressing lesion. Six patients died in the first two weeks after operation of pulmonary embolism, cardiac failure, pulmonary oedema, and of uncertain cause in the remainder. The total operative mortality was 6 per cent.

Results

By the very nature of the diseases under consideration cure is unlikely. Nineteen patients remain alive a year or more after treatment (Table I), of whom only three have survived five years. Prolongation of life must be an aim of therapy provided that such gain as is achieved is worth while. Though pain was often a presenting symptom, it was a major complaint in only a minority of patients. In these individuals operation

rarely improved this symptom, though subsequent radiotherapy was more often successful in this respect. In all patients the greatest threat to life and well-being were the dangers of a complete cord lesion.

Improvement in neurological function or arrest of deterioration for a satisfactory period of time should be the prime objective of therapy. There are apparent clinical criteria of neurological improvement. The patient should be able to walk and should have control of his sphincters. A more difficult problem is the determination of a satisfactory period of time for such improvement to last. This must be long enough to justify the pain, discomfort, and risks of surgical and other forms of treatment. In this series this problem was made easy by the fact that most patients in whom no recovery or further neurological deterioration took place died within six months. The cause of death appeared to be a general deterioration of health, as often due to chronic renal infection and pressure sores as to the primary disease. A little under a third of the patients in the entire series (Table I) were regarded as having satisfactory results, surviving more than six months, while over the same period of time they were ambulant and retained sphincter control. The remainder were regarded as failures, though four patients achieved a partial neurological recovery for a shorter period of time. In eight instances the follow-up details were inadequate, but, since all these patients showed complete neurological lesions when last seen, they were regarded as failures.

In only one-third, therefore, did the results appear to justify the treatment given. This rather discouraging fact prompted an analysis of the series to determine prognostic factors. From Table I the effect of histological pattern is clearly seen. Patients with myeloma or Hodgkin's disease or those with carcinoma of the breast or prostate had an even chance of a successful result, whereas only two patients with carcinoma of the bronchus did well. This may be related to the fact that other effective forms of treatment—that is, radiation and hormone therapy—exist for the former disorders. Other, as yet undiscovered, local factors must be operative as even temporary improvement following operation rarely occurs in the latter disease. Again the more slowly advancing lesions with a longer history had a better prognosis both in length and quality of survival. This is demonstrated in Table III where the patients have been divided into three categories: (1) those with spinal-cord symptoms of over one month's duration; (2) those with symptoms of under one month; (3) those patients in whom loss of cord function appeared within a few hours.

TABLE III.—*Results Classified According to Duration of Spinal-cord Involvement*

Duration of Spinal-cord Symptoms	No.	Satisfactory Results	% Success
Over 1 month	49	25	50
Under 1 month	66	18	27
Abrupt (within a few hours)	30	1	—
Total	145	44	—

This last group is of particular interest, since only a small proportion were related to vertebral collapse and probably a vascular incident caused the sudden loss of function. Here the only patient to make a satisfactory recovery was one in whom operation was carried out within four hours of the incident occurring. Complete vertebral collapse was not necessarily associated with a poor result, in that of 19 patients in whom this was present seven did reasonably well.

The severity of the neurological lesion had considerable bearing on the final results. Table II shows the results obtained classified according to the clinical sub-divisions already described. No patient in whom deep pain sensation was lost and who otherwise showed no sign of spinal-cord function below the lesion made any significant degree of recovery. The remaining patients demonstrated a direct correlation between the degree of cord damage and the final result. Early diagnosis and immediate treatment of spinal-cord compression appears to offer the only hope of improving the outlook for these unfortunate individuals.

As an index of the severity of a spinal-cord lesion, loss of sphincter control influenced the results but not to the same extent as other factors (Table IV). Though two-thirds of the patients without sphincter involvement made a satisfactory recovery, one-fifth of these in whom bladder function had been absent for seven days or more subsequently regained control.

TABLE IV.—*Results Classified According to Duration of Sphincter Loss*

Duration of Sphincter Loss	No.	Regained Control
No involvement	52	31
Under 48 hours	30	8
2—7 days	34	6
Over 7 days	29	5
Total	145	50

TABLE V.—*Results Classified According to Type of Lesion Found at Operation*

Type of Lesion Seen at Operation	No.	Satisfactory Result
Single: "Cuff"	52	14
Plaque or Mass:		
Anterior	26	5
Posterior	27	15
Lateral	23	7
Multiple	4	1
Unspecified	13	2
Total	145	44

The relationship of the tumour mass to the spinal theca provided a further factor in prognosis. This may be related to ease of surgical access or more probably to a number of local factors, such as blood supply to the spinal cord. Thus patients with posteriorly placed lesions progressed more favourably than those with anteriorly placed lesions. Of the five patients with anteriorly placed lesions who made a satisfactory improvement all had only a mild pre-operative neurological deficit. No patient with a severe neurological deficit due to an anteriorly placed or cuff-like lesion improved. There were four patients with multiple lesions seen at operation and in only one instance, a patient with myeloma, was a satisfactory result achieved. Since there was a fairly close correlation between the myelographic appearances and the operative findings this investigation has prognostic as well as diagnostic value.

No patient in whom there was clinical or simple radiological evidence of widespread metastases other than bony or skin involvement lived long enough to benefit significantly from treatment.

Discussion

A number of prognostic factors can therefore be derived from this study. Clearly in any one patient several factors may be inter-related. For instance, a patient with a slowly progressive carcinoma of the breast may have a circumscribed lesion lying posterior to the spinal cord, giving rise to a moderate neurological deficit. The patient is almost certain to do well. Another patient with an anteriorly placed metastasis from a carcinoma of the bronchus, producing a sudden paraplegia, will as certainly do badly. Between these extremes many combinations of the factors mentioned will be seen. Some guide to more favourable types of lesion and some improvement can be sought in an otherwise unpromising disorder.

Patients harbouring slowly growing tumours or tumours of the reticulo-endothelial system are likely to do well provided they have not progressed to a complete neurological lesion. Those with less favourable tumours will do badly, though the results may be improved by earlier and more vigorous treatment. Most of the patients with carcinoma of the bronchus in this series presented with severe or complete spinal-cord lesions. In such rapidly growing tumours speed of decompression of the cord is of vital significance to the final result. Similarly patients suffering abrupt spinal-cord lesions are unlikely to improve unless operated on within a few hours of the incident occurring. Patients with tumours situated on the posterior aspect of the theca will often do well, while anterior compression is of more sinister significance. No significant improvement by any form of therapy can be expected in patients who have suffered a complete spinal-cord lesion even if caused by the most favourable of these malignant tumours. Patients who show clinically obvious visceral metastases are unlikely to live long enough to benefit from treatment. Loss of bladder function even for several days does not necessarily indicate a poor prognosis.

No assessment of the relative merits of various forms of therapy can be given. All the patients under consideration were treated by a laminectomy soon after admission, often followed by other appropriate measures, including irradiation and hormone and chemical therapy. Many patients showing little improvement after laminectomy did not receive further treatment. There was no standard pattern from which conclusions could be drawn.

Surgery has the advantages of providing rapidly both a histological diagnosis and a decompression of the spinal cord. It also enables the clinician to distinguish with certainty between the diseases under consideration and other more benign forms of spinal-cord compression. It can do no more; the treatment of the underlying disease is in the hands of the radiotherapist or physician.

Summary

A series of 145 patients with spinal-cord compression from verified extradural malignant tumours has been presented. All were treated by laminectomy, often supplemented by other forms of treatment.

There was an operative mortality rate of 6%. Ten patients deteriorated after operation. Forty-four patients improved sufficiently and for an adequate period of time to justify the treatment given. Various prognostic factors are discussed.

Earlier diagnosis and treatment appear to offer the only hope of improving a rather unsatisfactory position.

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Prevention of Colds by Vaccination Against a Rhinovirus

A Report by the Scientific Committee on Common Cold Vaccines*

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Rhinoviruses can be isolated from 20 to 30% of adults with common colds (Hamre and Procknow, 1963), and therefore a successful rhinovirus vaccine would be a significant means of protection against this disease. Previous work at the Common Cold Research Unit has shown that specific antibody production can be stimulated by live or formalin-inactivated M strain rhinoviruses[1] (Doggett *et al.*, 1963), but it was not shown how long this antibody persisted or whether it would prevent colds. As there are many strains of rhinoviruses which are serologically distinct, a polyvalent vaccine would be necessary to ensure protection against infection with these viruses. Attempts have therefore been made to show that vaccination with a rhinovirus confers specific immunity to infection, and also to concentrate virus, and to enhance antibody responses by combining virus with adjuvant in the hope of finding a method by which several viruses might be concentrated into a small volume of inoculum and produce a large antibody response.

Materials and Methods

Three M strain rhinoviruses were used in the experimental vaccines—namely, H.G.P., and a serologically identical strain,

* The members of the Committee are: Sir Christopher Andrewes (chairman), Dr. D. A. J. Tyrrell (secretary) (M.R.C. Common Cold Research Unit), Dr. P. B. Stones (Pfizer Limited), Dr. A. J. Beale and Dr. R. D. Andrews (Glaxo Group Limited), Dr. D. G. ff. Edward and Dr. A. P. Goffe (Wellcome Foundation Limited), Miss Jennifer E. Doggett (M:R.C. Common Cold Research Unit), Dr. R. F. Homer and Mr. R. S. Crespi (National Research Development Corporation), Dr. E. M. B. Clements (Medical Research Council).
The report was prepared by Miss J. E. Doggett.
The Common Cold Vaccine Scientific Committee is the body which co-ordinates the research work being undertaken in this field within the previously announced collaboration between the Medical Research Council, Glaxo Group Limited, Pfizer Limited, the Wellcome Foundation Limited, and the National Research Development Corporation.

[1] M strain rhinoviruses grow in monkey-kidney cells in addition to human embryonic tissue and human malignant cells, in contrast with H strain rhinoviruses, which grow only in human embryonic tissues and human malignant cells. The virus originally described as E.C.H.O. virus type 28 is now agreed to be an M rhinovirus and not an enterovirus; the original name is retained in this paper as no alternative name has yet received general approval.