For Debate . . .

Differences between neurological and neurosurgical approaches in the management of malignant brain tumours

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Abstract

The management and outcome in 205 patients diagnosed as having cerebral gliomas over five years were reviewed. Patients referred to neurologists and neurosurgeons had similar clinical features and similar results on computed tomography. Patients referred to neurologists underwent burr hole biopsy less often and had better short term morbidity than patients referred to neurosurgeons, although final outcome was the same in both groups. Few patients underwent other surgical procedures. Referral for radiotherapy was usually by neurosurgeons, although this did not significantly affect long term survival.

The implications for the management of patients with primary malignant brain tumours and the need for prospective studies are discussed.

Introduction

Medical neurologists differ from their neurosurgical colleagues in their approach to the management of patients with malignant primary brain tumours. Neurologists tend to be more selective in choosing patients for biopsy. Accordingly, we set out to compare the practices of two neurologists and two neurosurgeons, who all considered themselves to take a fairly conservative approach to the management of malignant glioma.

Methods

A study was made of patients according to which of the four of us (DWC, PMF, MDMS, IRW) they had been initially referred to by other physicians. All reports on computed tomography over the five years 1978-82 were reviewed retrospectively. All computed tomography was undertaken with an EMI 1010 machine. The case notes of all patients whose results on computed tomography raised any possibility of the diagnosis of a primary brain tumour were then reviewed. Those patients in whom a primary malignant brain tumour was diagnosed on the basis of clinical results and findings on computed tomography were included in the study. Patients with proved primary malignancies elsewhere or multiple intracerebral lesions or in whom the diagnosis of cerebral abscess was considered even a remote possibility were excluded. Also excluded were all patients in whom there was any reasonable possibility of a benign tumour. The policy of both the surgeons and the physicians was that such patients should undergo open craniotomy.

Two hundred and twelve patients were identified and their outcome up to July 1984 determined. This necessitated writing to general practitioners, family practitioner committees, the Clatterbridge cancer registry, and the central registry of births, deaths, and marriages. Complete follow up was made in 205 patients, who formed the basis of this study. Patients were grouped according to whether initial referral had been to a neurosurgeon (MDMS or PMF) or neurologist (DWC or IRW). They were then compared with respect to age, sex, clinical features, results of computed tomography, management, current clinical state, and time to death. Clinical state when first admitted (including Glasgow coma scale rating[1]) and outcome on leaving hospital (Glasgow outcome scale[2]) were compared.

Statistical analysis of results was carried out using χ^2 tests and $p<0{\cdot}05$ was taken as significant. Survival times were compared using actuarial methods, and Kaplan-Meier graphs were plotted. These methods were used as a test of association between prognostic factors and outcome. As the study was not randomised and prospective they do not prove a causal relation.

Results

COMPARISON OF PATIENTS REFERRED TO NEUROLOGISTS AND NEUROSURGEONS

No difference in age, sex distribution, or duration of symptoms was encountered between the two groups. The incidence of headache, seizures, impaired consciousness (as determined by the Glasgow coma scale), papilloedema, or focal neurological signs did not differ significantly. The sites of the lesions and appearances on computed tomography were also the same for both groups (tables I-III). Few patients had angiography (nine in each group).

TREATMENT

Treatment, however, did differ (table IV). Almost all of the patients were treated with steroids. Significantly fewer patients in the group referred to neurologists underwent surgery ($p<0{\cdot}001$). Burr hole biopsy was the main surgical procedure carried out; other operations were craniotomy with biopsy, extensive excision of tumour, and shunt procedures. Histological reports were available for 130 of the patients, mainly from the surgical group and mostly from material obtained at biopsy (table V). Of the remaining patients, most died at home, and a postmortem examination was not carried out. The distribution of tumour types, classified histologically, was the same for both referral groups. One patient referred to neurologists had metastatic disease and another proved to have an acoustic neuroma. Two patients

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referred to a neurosurgeon had metastatic disease, and in two others histological examination showed a meningioma in one and a blood clot in the other.

The outcome at the point of leaving hospital differed, with more patients in the group referred to neurosurgeons having died or leaving hospital in a persistent vegetative state. Patients referred to neurologists were more likely to leave hospital with only moderate or lesser disability as assessed by the Glasgow outcome scale ($p<0·05$) (table VI). Nevertheless, differences in management made no difference in the overall survival time for patients (fig 1).

A number of factors appeared to influence the decision to submit patients to surgery. If patients had hydrocephalus ($p<0·05$) and were aged below 60 ($p<0·05$) they were more likely to undergo surgery. The site of the tumour was also influential. All patients with lesions of the posterior fossa underwent some form of surgical procedure, except for those with lesions affecting the brain stem. Of the patients who initially saw a neurologist, those referred for surgery more often presented with headache or papilloedema ($p<0·05$). They were more likely to have occipital or cerebellar lesions. Furthermore, the recording of focal neurological signs meant that patients were less likely to be referred for surgery ($p<0·05$). None of these differences held for the group referred to neurosurgeons, although a computed tomogram showing a poorly enhancing lesion or one with ring enhancement significantly increased the likelihood of operation.

Comparing burr hole biopsy and other forms of surgery is difficult as the latter was carried out in only 27 cases. Patients undergoing other procedures did not appear to do worse after operation and included more long term survivors.

More men than women were referred for radiotherapy. Those patients selected for radiotherapy more often had an unimpaired level of consciousness and no mental changes when first seen. Referral for radiotherapy was initiated by the neurosurgeon in almost all cases, even those originally referred to neurologists. Despite this, long term survival did not differ significantly, although there was a trend to improved survival with radiotherapy (fig 2).

In this study 18 patients survived more than three years from presentation. The histological diagnoses in these cases are shown in table V. Most of these patients were aged under 50; 10 underwent only burr hole biopsy, six underwent craniotomy and internal decompression or biopsy, and two had no surgical procedure.

The most important factor associated with prolonged survival time appeared to be age at diagnosis ($p<0·001$) (fig 3).

TABLE I—*Patient characteristics according to initial referral. Figures are numbers (%) of patients*

	Neurological approach (n=91)	Neurosurgical approach (n=114)
Sex:		
Men	49 (54)	60 (53)
Women	42 (46)	54 (47)
Age (years):		
<20	4 (4)	1 (1)
21-40	11 (12)	14 (12)
41-60	34 (38)	56 (49)
>60	42 (46)	43 (38)

TABLE II—*Presenting symptoms and signs. Figures are numbers (%) of patients*

	Neurological approach (n=91)	Neurosurgical approach (n=114)
Duration of symptoms (months):		
<1	2 (2)	7 (6)
1-2	3 (3)	10 (9)
2-6	30 (33)	40 (35)
6-12	24 (27)	16 (14)
>12	32 (35)	41 (36)
Types of symptom:		
Headache	61 (67)	79 (69)
Seizures	29 (32)	32 (28)
Mental changes	40 (44)	63 (56)
Papilloedema	29 (32)	47 (41)
Focal signs	77 (85)	87 (76)
Impaired consciousness (Glasgow coma scale <14)	24 (26)	33 (29)

TABLE III—*Appearance of brain tumour on computed tomography. Figures are numbers (%) of patients*

	Neurological approach (n=91)	Neurosurgical approach (n=114)
Site:		
Frontal	21 (23)	26 (23)
Temporal	18 (20)	25 (22)
Parietal	28 (31)	36 (31)
Occipital	5 (5)	8 (7)
Cerebellar	4 (4)	2 (2)
Brain stem	6 (7)	2 (2)
Bilateral	8 (9)	10 (9)
Basal ganglia	1 (1)	5 (4)
Calcification	2 (2)	8 (7)
Shift	78 (86)	100 (88)
Cystic	15 (16)	23 (20)
Ring enhancement	37 (41)	50 (44)
Hydrocephalus	45 (5)	7 (6)

TABLE IV—*Treatment and outcome. Figures are numbers (%) of patients*

	Neurological approach (n=91)	Neurosurgical approach (n=114)
Steroids	83 (91)	109 (96)
Surgery:		
None	48 (53)	24 (21) $p<0·001$
Burr hole biopsy	28 (31)	78 (68) $p<0·001$
Craniotomy and biopsy	4 (4)	2 (2)
Craniotomy and decompression	11 (12)	8 (7)
Shunt and biopsy	0 (0)	2 (2)
Radiotherapy after surgery	26 (29)	64 (56) $p<0·05$
Radiotherapy without surgery	1 (1)	2 (2)
Chemotherapy	5 (6)	5 (4)

TABLE V—*Histology. Figures are numbers (%) of patients*

	Neurological approach (n=46)	Neurosurgical approach (n=92)	Subjects surviving three years (No)
Normal brain	3 (7)	8 (9)	3
Necrotic tissue	1 (2)	5 (6)	3
Glioma (unspecified)	16 (35)	24 (26)	5
Astrocytoma grades I and II	8 (17)	11 (12)	6
Astrocytoma grades III and IV	13 (29)	37 (40)	6
Ependymoma	2 (4)	2 (2)	2
Oligodendroglioma	1 (2)	1 (1)	1
Other	2 (4)	4 (4)	1

TABLE VI—*Glasgow outcome scale at discharge. Figures are numbers (%) of patients*

	Neurological approach (n=91)	Neurosurgical approach (n=114)
Died	10 (11)	17 (15)
Persistent vegetative state	4 (4)	13 (11)
Severe disability	53 (58)	61 (54)
Moderate disability	19 (21)	10 (9)
Good recovery	5 (6)	13 (11) $p<0·05$
Final outcome:		
Alive, independent	6 (7)	5 (4)
Alive, dependent	5 (5)	5 (4)
Died	80 (88)	104 (92)

Discussion

Neurologists and neurosurgeons generally agree that all patients with a history and signs of cerebral tumour or abscess in whom appearances on computed tomography suggest a benign lesion, however remotely, demand craniotomy and exploration. Such

patients have not been included in this study. Disagreement exists for those patients in whom computed tomography appearances suggest a glioma of one form or another. This report is a clinical audit and as such offers no definite solutions to the dilemmas faced by neurologists and neurosurgeons in managing patients. We wish to raise important questions about management strategies in patients with probable primary cerebral tumours.

The survey shows that a broadly similar population of patients were referred to neurologists and neurosurgeons within the Mersey region. We cannot say what factors influence whether initial referral is to a neurophysician or neurosurgeon but it is most likely that chance is dominant. This survey confirms our suspicions that neurologists and neurosurgeons manage similar patients in different ways but that these differences have little impact on what is unfortunately an extremely bleak prognosis. The data do, however, suggest that the short term morbidity in patients initially referred to neurologists is rather less, and this may indicate a better quality of survival overall for patients initially referred to a neurologist. It seems most likely that these differences are due to the higher incidence of burr hole biopsy in the group referred to neurosurgeons. Others have noted the adverse effects of biopsy on patients' survival,[3-6] and our results would not support the suggestion that burr hole biopsy can be performed with a very low complication rate.[7]

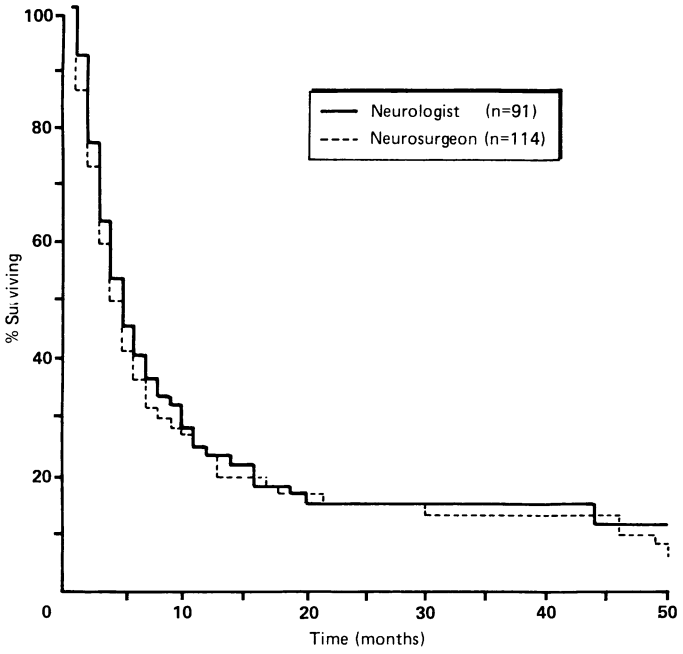

Fig 1—Effect of initial referral on survival.

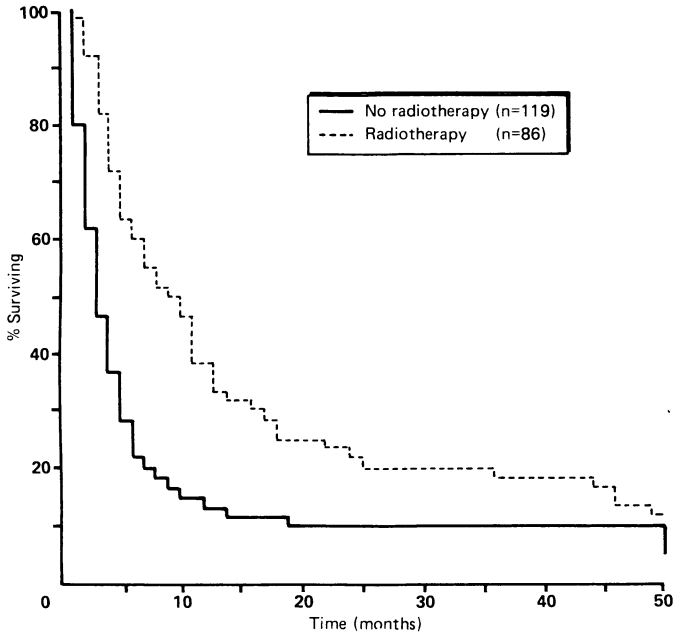

Fig 2—Influence of radiotherapy on survival.

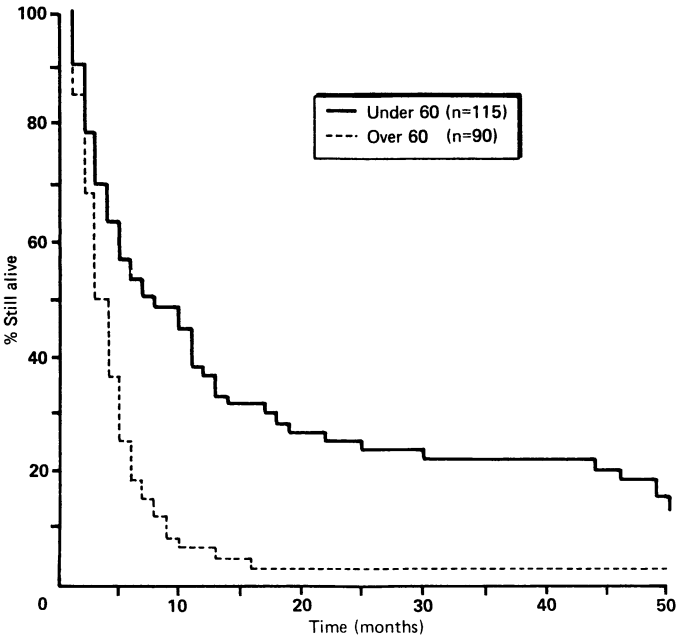

Fig 3—Influence of age at presentation on survival.

It is interesting to compare those factors which seem to influence management decisions made by neurophysicians and neurosurgeons. Our data suggest that neurophysicians were more easily convinced of a diagnosis on the basis of clinical findings and computed tomography than their neurosurgical colleagues and that in other than exceptional circumstances all that they offered as treatment was steroid therapy to reduce cerebral oedema. In contrast, neurosurgeons thought that histological verification was necessary, except under exceptional circumstances, but only rarely was the clinical and computed tomographic diagnosis altered in those who underwent biopsy. Neurosurgeons were much more likely to suggest subsequent radiotherapy than their neurological colleagues. Similarly, the factors that appeared to influence neurologists and neurosurgeons towards surgical treatment differed in some instances. Clinical factors such as the presence of headache and papilloedema without clear cut localising neurological signs were important in initiating neurosurgical treatment for patients initially referred to a neurologist. The appearances on computed tomography, however, influenced neurosurgeons to a greater degree than they did neurologists.

Many more patients referred to neurosurgeons underwent burr hole biopsy than those referred to neurologists, but a similar number of patients in each group had other surgical procedures, including craniotomy with biopsy and resection and ventriculoperitoneal shunting. Thus there seems less disagreement between neurologists and neurosurgeons concerning those patients who require surgical procedures other than burr hole biopsy.

Although our data may be taken as an argument for a more conservative approach to the need for confirming the diagnosis by histological examination, this has to be qualified. There is abundant evidence that clinical appearances and computed tomograms of cerebral mass lesions can be misinterpreted. We have direct evidence that this occurred in at least six (3%) of our cases. Although in half of these metastatic tumours were mistaken for primary brain

tumours, the other three were an acoustic neuroma, a meningioma, and a haematoma. Because we do not have histological confirmation in all cases other mistakes may have occurred. The need for biopsy whenever doubt arises is underlined by the fact that even two conservative neurologists felt that histological confirmation or more definitive surgical treatment was necessary in 47% of the cases referred to them. Furthermore, we would emphasise that follow up of patients who do not undergo biopsy is essential as an unexpected clinical course will necessitate full reappraisal. No cerebral abscesses were shown to have been misdiagnosed as gliomas in the survey, possibly because of the high index of suspicion and policy of reporting undertaken by experienced neuroradiologists. In this study we excluded any patients in whom the possibility of cerebral abscess or benign tumour was raised in the radiological report.

Our data do not allow us to make any positive statements about other means of management. Patients who received radiotherapy showed a trend towards longer survival. We cannot determine, however, whether this was an effect of treatment or whether patients with less severe problems and a younger age were referred for radiotherapy. We agree with others that the effects of radiotherapy are unlikely to be great,[8] and treatment carries with it fairly considerable adverse effects that may occupy an appreciable proportion of a patient's short period of survival. The survival times for our patients were very similar to those studied by other groups, including those who carried out extensive excision before administering radiotherapy and chemotherapy to all their patients.[8,9]

Too few patients had extensive tumour resection (particularly supratentorial tumour resection) for us to comment on this aggressive approach to the management of tumours in our patients. Such resections can, however, be regarded only as palliative,[10] and our study appears to show that a small subgroup of patients with astrocytomas survive for long periods without aggressive treatment.

Thus in the end clinicians must make a finely balanced clinical judgment. Do they accept the small risk of missing a surgically treatable lesion, such as benign tumour, so that more patients have a better quality of life during their limited time span, or do they subject most patients to some form of biopsy procedure with the inevitable morbidity and mortality that this entails?

Clinicians will continue to face the dilemmas illustrated by this short survey as long as satisfactorily controlled prospective studies of the treatment of primary malignant brain tumours remain unavailable. We would like to suggest from our data that a conservative approach to management with steroids alone can be justified ethically. It would, therefore, seem reasonable that future studies could include a comparative control group of patients randomised to such management. We believe that it is only by adopting this approach that we will be able to improve the care of these patients.

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What evidence is there that megadoses of vitamin D prevent chilblains?

Chilblains (pernio) are a form of cold injury of the skin of the "slow freeze" variety. They consist of bluish red itchy lumps, usually on the dorsum of the fingers and toes which may, in severe cases, break down to form shallow ulcers. They most commonly occur in thin young women who also have acrocyanosis—that is, cold purple/blue hands and feet—and who live in cold damp houses in cold damp climates. They are worse in winter and usually clear away in the summer except in more northern climates. The most important investigation in these patients is to ask them how much their fuel bills were in the winter, and it is often amazing how little these people spend on heating, indicating that they live in a freezing environment. Evaluation of any treatment is difficult because of the chronic variable unpredictable nature of the lesions. Thus most treatments have not been subjected to any adequate testing. I know of no evidence that megadoses of vitamin D are of any help, and indeed would regard it as irresponsible to use such a treatment, with its risks of hypercalcaemia and metastatic calcification. The only cure is to go and live in a hot country but this is not usually feasible for most patients. Scrupulous attention to keeping themselves warm by wearing adequate clothing and keeping the home and workplace warm is essential. In severe cases electrically heated socks and gloves may be of great value. Sportsman's hand warmers of the charcoal stick or chemical variety also help. Vasodilators are, in my experience, of little benefit and side effects are a problem. For acrocyanosis and pernio of the feet, lumbar sympathectomy by phenol injection is often of great value, though the effect may wear off after a few years, but it may then be repeated.—E HOUSLEY, consultant vascular physician, Edinburgh.

When should adrenalectomy be done for Cushing's syndrome? Will adrenalectomy stop or reverse osteoporosis and is there any medical treatment for osteoporosis?

Adrenalectomy is the treatment of choice for Cushing's syndrome when it is due to an adrenal tumour. Cushing's syndrome may also be due to ectopic production of adrenocorticotrophic hormones from a non-endocrine tumour when the source is usually a bronchial carcinoma or carcinoid. The treatment of choice is then the removal of the tumour and if this is not possible metyrapone, an inhibitor of the hydroxylation of deoxycortisol to cortisol, may reduce the production of cortisol. The term Cushing's disease is reserved for those cases of Cushing's syndrome due to bilateral adrenal hyperplasia secondary to excessive production of adrenocorticotrophic hormones by the pituitary. For Cushing's disease the favourite treatment 15 years ago was bilateral adrenalectomy followed by replacement therapy with cortisol and fludrocortisone. Unfortunately some patients developed Nelson's syndrome with increased pigmentation due to excess production of adrenocorticotrophic hormones and enlargement of the pituitary tumour. Recently trans-sphenoidal or transfrontal removal of the pituitary tumour has been preferred. Some centres favour external irradiation of the pituitary or implant of yttrium-90 into the pituitary. Nevertheless, there are still centres practising bilateral adrenalectomy for Cushing's disease and a recent report from Manchester maintains that it is still a satisfactory treatment.[1] A recent review of 18 years' experience in managing Cushing's disease concludes that adrenalectomy is less than ideal.[2] The authors favour pituitary irradiation in the young, and resection of the pituitary tumour in adults appears to be the best present form of treatment. Removal of the cause of the excess production of cortisol will reverse the osteoporosis. Calcium supplements prevent deterioration in patients with osteoporosis. Oestrogens will improve the calcium balance and reduce the rate of bone reabsorption in postmenopausal women. A combination of hormone replacement therapy and one alpha 1 μg daily has been recommended.[3] In men calcium supplements and one alpha are advisable. Anabolic steroids, sodium fluoride, and calcitonin have been recommended but evidence for any beneficial effect is still unconvincing.—C W H HAVARD, consultant physician and endocrinologist, London.

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