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Short communication

Glioblastoma in the elderly — How do we choose who to treat?

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ABSTRACT

Objective
Glioblastoma (GBM) is the commonest primary malignant brain tumour amongst the adult population. Incidence peaks in the 7th and 8th decades of life and as our global population ages, rates are increasing. GBM is an almost universally fatal disease with life expectancy in the range of 3–5 months amongst the elderly.
Materials and Methods
The assessment of elderly GBM patients prior to treatment decisions is poorly researched and unstandardised. In order to begin tackling this issue we performed a cross-sectional survey across all UK based consultant neuro-oncologists to review their current practice in assessing elderly GBM patients.
Results
There were 56 respondents from a total of 93 recipients (60% response rate). All respondents confirmed that at least some patients aged 70 or over were referred to their clinics from the local multidisciplinary team meeting (MDT). Only 18% of consultants routinely performed a cognitive or frailty screening test at initial consultation. Of those who performed a screening test, the majority reported that the results of the test changed their treatment decision in approximately 50% of cases. Participants ranked performance status as the most important factor in determining treatment decisions.
Conclusions
Considering the heterogeneity of this patient population, we argue that performance status is a crude measure of vulnerability within this cohort. Elderly GBM patients represent a unique clinical scenario because of the complexity of distinguishing neuro-oncology related symptoms from general frailty. There is a need for specific geriatric assessment models tailored to the elderly neuro-oncology population in order to facilitate treatment decisions.

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1. Introduction

Glioblastoma (GBM) is the commonest primary malignant brain tumour amongst the adult population with approximately 2000 new cases diagnosed in the UK per year. Incidence peaks in the 7th and 8th decades of life and as our global population ages, rates are increasing. Outcomes from this disease remain poor with median life expectancy in England at 6.1 months, dropping to 3.2 months amongst those aged over 70.[1]

Given the poor prognosis in this group, treatment must be balanced against side effects and worsening quality of life. Treatment in those under 70 was standardised by the landmark EORTC 26981 trial, showing a 2 month survival benefit and a doubling of 2 year survival rates with concurrent radiotherapy (RT) and temozolomide (TMZ) chemotherapy followed by 6 months of adjuvant TMZ. The age cut off for this trial was 70, however in the group of trial patients over the age of 65 the benefit of adding chemotherapy to radiotherapy was not statistically significant.[2] There is concern that long course chemotherapy and radiotherapy may in fact be detrimental to elderly and frail patients.

In patients aged 70 or over there is a lack of consensus on standard of care. Radiotherapy has a survival advantage over best supportive care[3] however the optimal dose of radiotherapy is yet to be established with a recent International Atomic Energy Agency study suggesting non-inferiority of shorter regimes in the palliative setting.[4] A recent Phase III trial randomised elderly GBM patients to standard radiotherapy with 60 Gy in 30#, hypofractionated radiotherapy of 34 Gy in 10# or TMZ chemotherapy alone. For patients older than 70, survival was significantly longer with TMZ or hypofractionated radiotherapy than with standard radiotherapy.[5] Those with defects in the DNA repair protein MGMT did significantly better in the chemotherapy arm than those with intact MGMT, a result which was replicated in the NOA-08 trial which randomised elderly GBM patients to standard radiotherapy with 60 Gy in 30# or TMZ alone. This non-inferiority trial showed TMZ to be a suitable monotherapy option, with greater effect seen in those with MGMT promoter methylation.[6] There is now evidence to support the use of chemotherapy or radiotherapy as single agents amongst elderly GBM patients and an increasing interest in using MGMT promoter methylation status as a biomarker. However there remains a paucity of data surrounding the clinical basis by which individual patients are assessed for treatment.

Assessment of older patients with GBM is challenging due to the mix of tumour-related symptoms and pre-existing comorbidities, and it can be difficult to predict which patients will benefit from active treatment. Multi-dimensional geriatric assessment has been shown to predict for tolerance to treatment and survival in other tumour types.[7] It is apparent that the assessment tools used in oncology patients with extra-cranial malignancies are likely to be less valid within the GBM cohort because of the unique and potentially isolated deficits caused by the disease itself. As yet there is a paucity of trial data assessing the benefit of geriatric assessment in determining treatment options and providing a prognostic scoring system amongst elderly neuro-oncology patients. In order to begin addressing this issue we performed a cross-sectional survey of all UK based consultant neuro-oncologists, to review their current practice in assessing elderly GBM patients.

2. Materials and Methods

2.1. Study Design

A short cross-sectional survey design was used. Data were collected from November to December 2015.

2.2. Participants

The survey aimed to capture the views of all currently practising consultant neuro-oncologists in the UK. Consultant neuro-oncologists were defined by practice patterns and attendance at local MDTs and were identified from conference attendances, The Brain Tumour Charity database and direct telephone contact with secretaries working at all of the oncology centres within the UK. E-mail addresses were collated and a link to the online survey sent to each. 93 participants were identified in total. Participants were excluded if not currently practising due to long term illness, maternity leave or having retired.

2.3. Questionnaire

The questionnaire was designed by the principal investigator and the validity of the questions assessed by 3 consultant co-investigators from 3 different centres. The survey was kept purposefully short in order to increase the likelihood of a high response rate. The first section aimed to assess the local referral systems for elderly GBM patients to oncology clinics. The second and third sections concentrated on how clinicians currently assess elderly GBM patients and how importantly they rank certain clinical, pathological and radiological characteristics (see Table 2). The final section assessed local access to multidisciplinary team support including physiotherapists, occupational therapists and speech and language teams within the outpatient setting.

2.4. Data Collection and Analysis

A link to the online survey was e-mailed to all participating consultant neuro-oncologists. 2 subsequent reminder e-mails were sent. As the survey was anonymised to prevent reporting bias, it was not possible to identify the non-responders to remind them further. Data was analysed using Microsoft Excel 2010.

2.5. Ethical Considerations

The survey was supported by The Brain Tumour Charity and the NCRI Brain Tumour Clinical Studies Group. No financial aid was given. The survey was voluntary, anonymous, aimed only at healthcare professionals and therefore was not considered to require IRB approval.

3. Results

3.1. Responses

There were 56 responders resulting in an overall response rate of 60%.

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