Clinical Study

Brain stem gliomas: Patterns of Care in Victoria from 1998–2000

Mark A. Rosenthal a,*, David M. Ashley b, Katharine J. Drummond c, Michael Dally d, Michael Murphy e, Lawrence Cher f, Vicky Thursfield f, Graham G. Giles g

a Department of Clinical Haematology and Medical Oncology, Royal Melbourne Hospital, Grattan Street, Parkville, Victoria 3050, Australia
b Children’s Cancer Centre, Royal Children’s Hospital, Parkville, Victoria, Australia
c Department of Neurosurgery, Royal Melbourne Hospital, Parkville, Victoria, Australia
d William Buckland Radiotherapy Centre, Alfred Hospital, Melbourne, Victoria, Australia
e Department of Neurosurgery, St Vincent’s Hospital, Melbourne, Victoria, Australia
f Department of Medical Oncology, Austin Health, Melbourne, Victoria, Australia
g Cancer Epidemiology Centre, Cancer Council of Victoria, Melbourne, Victoria, Australia

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Abstract

This study describes the management of and outcomes for adult and paediatric patients with newly diagnosed brain stem gliomas during 1998–2000 in Victoria. Adult patients were identified in a retrospective cohort study conducted by surveying doctors involved in managing incident brainstem glioma cases identified from the population-based Victorian Cancer Registry. Paediatric cases were identified from a retrospective analysis of the Victorian Paediatric Brain tumour database for the same period. Ten adult and 14 paediatric patients were considered eligible for this study. Nine (38%) did not have a histologic diagnosis but were diagnosed on the basis of radiological appearance. Complete macroscopic resection was performed in two patients (8%). A variety of tumour types and grades were observed with surgery and radiotherapy the mainstays of therapy. No adult patients and only eight (57%) paediatric patients received chemotherapy. The median survivals for adult patients, paediatric patients with pontine lesions and paediatric patients with non-pontine lesions were: 57, 10 and 60+ months respectively.

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1. Introduction

In Victoria in 2003, there were 346 cases of invasive primary brain and central nervous system cancer, with 341 deaths, making it the 8th most common cause of cancer-related death. The majority of these cancers are high-grade gliomas: glioblastoma multiforme (GBM), anaplastic astrocytoma and mixed anaplastic astrocytoma/oligodendroglioma. For patients with gliomas, poorer prognosis is associated with increasing tumour grade, older age, worse performance status and residual disease post-surgical resection.

A small but important group of patients are those with brainstem gliomas. Adult and paediatric patients with these rare tumours require specialist surgical care and a multidisciplinary approach to treatment. While there is much literature in the paediatric population, particularly related to the poor prognosis of diffuse pontine glioma, there is little reported information in the literature regarding the management of adult patients with these tumours and their outcomes remain uncertain. We have previously reported our findings in patients with gliomas and now present specific data regarding the subset of adult patients with brainstem gliomas and comparative paediatric data over the same period.

2. Methods

This paper reports patients of all ages diagnosed with a brain stem glioma between 1998 and 2000.
The methodology for this adult glioma survey has previously been published. In brief, a population-based sample of all adult patients with glioma diagnosed in Victoria during 1998, 1999 and 2000 was identified from the Victorian Cancer Registry. Treating clinicians were sent a questionnaire relating to the management of each patient. Eligible patients included those aged over 16 years, diagnosed with gliomas including low-grade gliomas, anaplastic tumours and GBM.

The questionnaire was designed to address specific issues, including: patient demographics, referral patterns and surgical, radiation and chemotherapy management. The questionnaire did not evaluate presenting symptoms and signs or diagnostic imaging practices.

A state-based paediatric cancer database is located at the Royal Children’s Hospital with details of patient demographics, and surgical, radiation and chemotherapy management. All patients between birth and 16 years of age diagnosed with a brainstem glioma in the state of Victoria between 1998 and 2000 were included for an analysis.

2.1. Statistical analysis

Descriptive statistics were analysed with the SPSS statistical package.

2.1.1. Ethical approval

The Cancer Council of Victoria Institutional Ethics Committee approved the survey proposal.

3. Results

3.1. Adult patients

From the period 1998–2000, 828 glioma cases were identified from the Victorian Cancer Registry. Of these, 10 adult patients were identified with brainstem gliomas (1.2%). Patient demographics are detailed in Table 1. There was a female preponderance and seven patients (70%) were aged less than 40 years.

Seven patients had a histological diagnosis. Tumour grade was determined in five patients (50%) and a further two patients (20%) had a diagnosis of glioma without a grade specified. Of the five patients with tumour grading, four were classified as having grade III and one as having a grade IV tumour. Three patients did not have a histological diagnosis due to: tumour location (2) and patient refusal (1). Table 1 details tumour classification.

3.1.1. Surgical considerations

Table 1 provides additional detail regarding surgical management. Seven patients underwent surgery. Of these, three underwent a biopsy only due to tumour location while the remaining four patients underwent craniotomy for tumour resection. Gross macroscopic resection was achieved in only one patient. Two patients (20%) underwent a further resection at tumour recurrence.

3.1.2. Referral patterns

According to the primary questionnaire, nine patients (90%) were referred to a radiation oncologist and two (20%) were referred to a neuro-oncologist at initial diagnosis. Of these, seven (70%) received radiotherapy but no patient received chemotherapy.

3.1.3. Survival

Two patients were known to have developed tumour recurrence. Fig. 1 shows the overall survival time for this patient group. The median survival was 57 months overall. Seven patients (70%) were alive at 5 years.

3.2. Paediatric patients

From the period 1998–2000, 14 paediatric patients were identified as having brainstem gliomas. Patient demographics are detailed in Table 1.

Nine patients had pontine gliomas and five patients had non-pontine brainstem tumours. Eight patients had a histological diagnosis, and tumour grade was determined in
six patients (43%) and a further two patients (14%) had a diagnosis of glioma without a grade specified. Of the eight patients with tumour grading, three (37%) were classified as having grade III or IV tumours. Six patients (43%) did not have a histological diagnosis due to tumour location. Table 1 details tumour classification.

3.2.1. Surgical considerations

Table 1 provides additional detail regarding surgical management. Eight patients underwent surgery. Of these, seven underwent a biopsy only due to tumour location. Gross macroscopic resection was achieved in only one patient.

3.2.2. Additional therapy

Of the 14 paediatric patients, seven (70%) received radiotherapy, eight (57%) received chemotherapy and four (29%) received both chemotherapy and radiotherapy. Of the nine patients with pontine gliomas, eight and four received radiotherapy and chemotherapy respectively. Of the five patients with non-pontine brain stem gliomas, three received chemotherapy and none received radiotherapy.

3.2.3. Survival

Overall, the median survival of the 14 paediatric patients with brainstem gliomas was 20 months (Fig. 2a). All patients with non-pontine brainstem gliomas were alive at 5 years while the median survival of patients with pontine gliomas was 10 months. Two patients are alive at 5 years. (Fig. 2b).

4. Discussion

This retrospective cohort study examined the management of 10 adult patients and 14 paediatric patients with brainstem gliomas treated over a 3-year period. Brainstem gliomas represent a small fraction of all gliomas in adults. In this survey, they represented only 1.2% of all adult gliomas.5 In the paediatric age group, brainstem gliomas represent up to 20% of all central nervous system tumours. In general, reports document the heterogeneity of pathological diagnosis, the limitations of surgery, the modest benefits arising from irradiation and the poor prognosis. The role of chemotherapy remains uncertain.7,11 The majority are diffuse intrinsic gliomas with a median survival of less than 12 months despite radiotherapy.7,9 Other brainstem tumours include: focal tectal gliomas, posterior exophytic gliomas and neurofibromatosis type 1-related tumours. In general, these subtypes have a better prognosis than the diffuse intrinsic group.9

In contrast to the paediatric literature, there is very little information regarding brainstem gliomas in the adult population. Epidemiological data suggest that they represent less than 2% of all adult gliomas and are a heterogeneous group of tumours.12–14 Adults with brainstem gliomas appear to have an improved prognosis compared with paediatric patients, particularly in those patients who have an absence of necrosis on MRI, low-grade histology and longer duration of symptoms (>3 months).12,14

The management of adult brainstem gliomas revolves around histology if available. In the study of 48 patients by Guillamo, only 71% had a histological diagnosis.12
The approach to high-grade tumours is clearly different from the approach to low-grade brainstem gliomas. Mursch et al. examined the role of micro-neurosurgical techniques in the treatment of 16 adult patients with intrinsic brainstem gliomas. Their review documented the difficulties associated with surgery and the perceived lack of benefit. The 5-year survival in their group of patients was 37%. Radiotherapy is routinely used in this group of patients but the role of chemotherapy remains uncertain.

Our study documents many expected features in these two patient groups. The majority of adult patients had anaplastic gliomas and 70% were aged less than 40 years. The general approach to management conformed to recent standards of care. That is, histological diagnosis was obtained, a macroscopic resection was performed if feasible and patients were referred for radiotherapy. Despite the preponderance of high-grade histology and limitations of therapy, the median survival was 57 months.

In contrast, the paediatric group population represented two distinct groups: pontine and non-pontine lesions. The former were generally higher grade tumours and had a very poor outlook with a median survival of only 10 months. On the other hand, the non-pontine lesions were generally of lower grade including pilocytic astrocytomas and the outlook was significantly better with all patients alive at 5 years.

Our study may be criticised on a number of levels. First, it is now over 8 years since some of these patients were diagnosed and treated and the management principles of the treating clinicians may have changed as imaging, surgical and radiotherapy techniques have improved significantly and new chemotherapy options such as temozolomide are now available. Second, the small numbers of patients in this retrospective review make data interpretation difficult. Third, we did not differentiate clearly in the adult patients as to the exact site of the lesion within the brainstem. This may or may not have prognostic ramifications, particularly given the paediatric data.

However, a number of observations were made. First, the extent of surgery was severely limited in both adult and paediatric groups by the tumour location. Nine patients (38%) did not have a biopsy and only two (8%) in the entire population had a macroscopic resection. The diagnosis of brain stem glioma was made through radiological assessment (MRI) in those patients who did not have a biopsy diagnosis. Second, no adult patients were enrolled in a clinical trial. Indeed, the diagnosis of a brainstem glioma almost always precludes a patient from a systemic therapy trial. Third, no adult patient received chemotherapy, a treatment that has a clear role in the treatment of intracerebral gliomas.

In conclusion, we have examined the characteristics and management of both adult and paediatric brainstem gliomas diagnosed over a 3-year period. Our findings are consistent with that of previous reports, highlight the difficulties associated with these tumours and identify variable outcomes. These remain complex cases and mandate a multidisciplinary approach to management.

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References