Presenting characteristics, histological subtypes and outcomes of adult central nervous system tumours: retrospective review of a surgical cohort

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Abstract

Introduction: The most recent local study on the incidence of histological subtypes of all brain and spinal tumours treated surgically was published in 2000. In view of the outdated data, we investigated the presenting characteristics, histological subtypes and outcomes of adult patients who underwent surgery for brain or spinal tumours at our institution.

Methods: A single-centre retrospective review of 501 patients who underwent surgery for brain or spinal tumours from 2016 to 2020 was conducted. The inclusion criteria were (a) patients who had a brain or spinal tumour that was histologically verified and (b) patients who were aged 18 years and above at the time of surgery.

Results: Four hundred and thirty-five patients (86.8%) had brain tumours and 66 patients (13.2%) had spinal tumours. Patients with brain tumours frequently presented with cranial nerve palsy, headache and weakness, while patients with spinal tumours frequently presented with weakness, numbness and back pain. Overall, the most common histological types of brain and spinal tumours were metastases, meningiomas and tumours of the sellar region. The most common complications after surgery were cerebrospinal fluid leak, diabetes insipidus and urinary tract infection. In addition, 15.2% of the brain tumours and 13.6% of the spinal tumours recurred, while 25.7% of patients with brain tumours and 18.2% of patients with spinal tumours died. High-grade gliomas and metastases had the poorest survival and highest recurrence rates.

Conclusion: This study serves as a comprehensive update of the epidemiology of brain and spinal tumours and could help guide further studies on brain and spinal tumours.

Keywords: Central nervous system, epidemiology, neoplasm, neuropathology, tumour

INTRODUCTION

Tumours of the brain and spine are rare. In Southeast Asia, the incidence rates of benign and malignant brain and spinal tumours were 6.97 and 3.29 per 100,000 person-years, respectively.[1] Globally, the most common malignant type of brain and spinal tumours is astrocytic tumours, with an overall incidence rate of 2.98 per 100,000 person-years.[2] Among adolescents and young adults, the 5-year survival of low-grade astrocytic tumours ranged from 71.4% to 93.4%, while the 5-year survival of high-grade astrocytic tumours ranged from 14.2% to 55.4%.[3] On the other hand, data on the incidence and outcomes of benign brain and spinal tumours globally are not as well reported, in part due to the different legislative requirements across countries on the reporting of benign brain and spinal tumours.[4]

Access this article online

Quick Response Code:

Website: https://journals.lww.com/SMJ

DOI: 10.4103/singaporemedj.SMJ-2022-069

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Received: 25 Apr 2022 **Accepted:** 24 Aug 2022 **Published:** 23 Aug 2023

How to cite this article: Lim MJR, Zheng Y, Eng SWO, Seah CWT, Fu S, Lam LZL, *et al*. Presenting characteristics, histological subtypes and outcomes of adult central nervous system tumours: retrospective review of a surgical cohort. Singapore Med J 0;0:0.

The literature on brain and spinal tumours in Singapore is limited. Recent local studies on the epidemiological characteristics of brain and spinal tumours examined only malignant types and subtypes, including primary malignant brain tumours,[5] high-grade gliomas[6] and glioblastoma.[7] The most recent study on the incidence of histological subtypes of all brain and spinal tumours treated surgically in Singapore was published in 2000.[8] Therefore, we aimed to summarise the presenting characteristics, histological subtypes, and surgical management and outcomes of brain and spinal tumours at our institution.

METHODS

This was a retrospective study of 501 consecutive adult patients who underwent surgery for brain or spinal tumours at our institution, a tertiary referral centre, from 2 January 2016 to 2 January 2020.

The operating theatre records database was accessed to retrieve the National Registration Identity Card numbers (NRICs; which act as the national identification number), operation date, provisional diagnosis, operation summaries and surgical codes of all patients who underwent surgery for a brain or spinal tumour. The medical records of 667 patients were retrieved and screened for inclusion in the study. The inclusion criteria were (a) patients who had a brain or spinal tumour that was histologically verified and (b) patients who were aged 18 years and above at the time of surgery. One hundred and twenty patients were excluded, as the histology report indicated that the lesion was not a tumour, and 46 patients were excluded as they were below the age of 18 at the time of surgery. Institutional ethics approval was obtained from the local institutional review board before the commencement of the study, and a waiver of informed consent was granted since this study posed no more than minimal risk to participants.

Clinical data were collected from the electronic medical records of all patients using a standardised data collection form. The variables collected included (a) demographics (including age at the time of surgery, sex, citizenship status and smoking history); (b) presenting signs and symptoms; (c) interventions administered (including resection, radiotherapy, chemotherapy, gamma knife radiosurgery, whole-brain radiotherapy and stereotactic biopsy with no subsequent resection); (d) complications from surgery; (e) histological diagnosis of the tumour as stated in the pathology report; (f) outcomes (including all-cause mortality and tumour recurrence as reported by the radiologist in the radiology reports of follow-up scans), duration of hospitalisation; and (g) duration of follow-up (defined as the duration in years between the date of admission for the first resection or stereotactic biopsy of the tumour, whichever was later, and the date of the most recent follow-up clinic visit).

Baseline characteristics of the patients were reported using mean and standard deviation (SD) for continuous variables that followed a normal distribution and median and interquartile range (IQR) for continuous variables that did not follow a normal distribution. Categorical variables were reported using count numbers and percentages. For selected histological types of brain and spinal tumours, time-to-event analysis of all-cause mortality and radiological evidence of tumour recurrence was performed using the Kaplan–Meier method and hypothesis testing was performed using the log-rank test. A P value ≤ 0.05 was taken to be statistically significant. For patients who did not die or did not have radiological evidence of recurrence during the follow-up period, the duration of follow-up was recorded instead for time to all-cause mortality and time to recurrence. The 11 patients (2.2%) who only had a stereotactic biopsy of the tumour with no subsequent resection were excluded from the analysis for time to recurrence. All data analyses were conducted using R Studio Version 1.2.5042 (RStudio, PBC, Boston, MA, USA).

RESULTS

Baseline demographics and patient characteristics

The demographics, past medical history, presenting signs and symptoms, and outcomes of patients with brain and spinal tumours are presented in Table 1. A total of 501 patients were included in the analysis. Of these, 435 (86.8%) patients had brain tumours and 66 (13.2%) patients had spinal tumours. The median (IQR) duration of follow-up was 518 (175, 940) days. The mean (SD) age of the study population was 53.3 (15.6) years, and 257 (51.3%) patients were female. Chinese patients made up 54.1% of the patients (271 patients). Most of the patients were never smokers (79.6%).

The most common presenting signs or symptoms of patients with brain tumours were cranial nerve palsy (149 patients, 34.3%), headache (141 patients, 32.4%) and weakness (90 patients, 20.7%). The median (IQR) duration of hospitalisation was 10 (6, 20) days. Brain tumour recurred in 66 (15.2%) patients and 112 (25.7%) patients died.

The most common presenting signs or symptoms of patients with spinal tumours were weakness (30 patients, 45.5%), numbness (29 patients, 43.9%) and back pain (27 patients, 40.9%). The median (IQR) duration of hospitalisation was 7 (5, 15) days. Nine (13.6%) patients had recurrence of spinal tumour and 12 (18.2%) patients died.

Characteristics of brain and spinal tumours

The histological types of brain and spinal tumours in our cohort are presented in Table S1 [see Supplemental Digital Appendix]. The 2016 World Health Organization Classification of Tumours of the Central Nervous System was used to classify the tumours.[9] A detailed breakdown of the histological *subtypes* can be found in Table S2 [see Supplemental Digital Appendix]. The five most common histological *types* of brain and spinal tumours overall were metastases, meningiomas, tumours of the sellar region, diffuse astrocytic and oligodendroglial tumours, and nerve sheath tumours.

Table 1. Demographics, presenting characteristics and outcomes of patients who underwent surgery for central nervous system tumours.

Variable	*n* (%)		
	Brain tumour (*n*=435, 86.8%)	Spinal tumour (*n*=66, 13.2%)	Total (*n*=501)
Age[a] (yr)	53.2±15.7	53.5±14.8	53.3±15.6
Female gender	222 (51.0)	35 (53.0)	257 (51.3)
Ethnicity			
Chinese	230 (52.9)	41 (62.1)	271 (54.1)
Malay	42 (9.7)	7 (10.6)	49 (9.8)
Indian	25 (5.7)	3 (4.5)	28 (5.6)
Others	138 (31.7)	15 (22.7)	153 (30.5)
Smoking status			
Never smoker	350 (80.5)	49 (74.2)	399 (79.6)
Previous smoker	45 (10.3)	9 (13.6)	54 (10.8)
Current smoker	40 (9.2)	8 (12.1)	48 (9.6)
Presenting signs and symptoms			
Cranial nerve palsy	149 (34.3)	0 (0.0)	149 (29.7)
Headache	141 (32.4)	1 (1.5)	142 (28.3)
Weakness	90 (20.7)	30 (45.5)	120 (24.0)
Gait abnormality	75 (17.2)	13 (19.7)	88 (17.6)
Dizziness	77 (17.7)	1 (1.5)	78 (15.6)
Nausea or vomiting	76 (17.5)	1 (1.5)	77 (15.4)
Numbness	33 (7.6)	29 (43.9)	62 (12.4)
Seizure	40 (9.2)	0 (0.0)	40 (8.0)
Back pain	10 (2.3)	27 (40.9)	37 (7.4)
Speech abnormality	34 (7.8)	1 (1.5)	35 (7.0)
Memory loss	26 (6.0)	1 (1.5)	27 (5.4)
Radiculopathy	6 (1.4)	20 (30.3)	26 (5.2)
Behavioural abnormality	20 (4.6)	0 (0.0)	20 (4.0)
Ataxia	16 (3.7)	1 (1.5)	17 (3.4)
Bladder dysfunction	10 (2.3)	7 (10.6)	17 (3.4)
Paraesthesia	11 (2.5)	3 (4.5)	14 (2.8)
Bowel dysfunction	8 (1.8)	6 (9.1)	14 (2.8)
Loss of consciousness	14 (3.2)	0 (0.0)	14 (2.8)
Loss of nociception	2 (0.5)	1 (1.5)	3 (0.6)
Duration of hospital stay[b] (day)	10 (6, 20)	7 (5, 15)	10 (6, 19)
Recurrence	66 (15.2)	9 (13.6)	75 (15.0)
Allcause death	112 (25.7)	12 (18.2)	124 (24.8)
Duration of follow-up[b] (day)	524 (141, 985)	471 (212, 829)	518 (175, 940)

[a]Data presented as mean±standard deviation. [b]Data presented as median (interquartile range).

The most common histological *types* of brain tumours were metastases (100 patients, 23.0%), meningiomas (98 patients, 22.5%) and tumours of the sellar region (90 patients, 20.7%). Brain tumours were mostly located at the cerebrum (243 patients, 55.9%), sellar region (98 patients, 22.5%) and cerebellum (71 patients, 16.3%).

The most common histological *types* of spinal tumours were nerve sheath tumours (31 patients, 47.0%), metastases (15 patients, 22.7%) and meningiomas (12 patients, 18.2%). Spinal tumours were mostly located at the thoracic (31 patients, 47.0%), lumbar (16 patients, 24.2%) and cervical (11 patients, 16.7%) spinal levels. Spinal tumours were intradural in 46 (69.7%) patients and intramedullary in seven (10.6%) patients.

Demographics of patients with selected histological types of brain and spinal tumours

The demographics of patients with selected histological types of brain and spinal tumours are reported in Table S3 [see Supplemental Digital Appendix]. Patients with primary central nervous system (CNS) lymphoma formed the oldest age group of patients, with a mean (SD) age of 63.3 (12.8) years, while patients with other astrocytic tumours formed the youngest age group of patients, with a mean (SD) age of 29.0 (13.6) years. The histological type with the greatest proportion of females

was meningiomas (73 patients, 66.4%), while that of males was mesenchymal, non-meningothelial tumours (10 patients, 71.4%). The most common histological type of brain and spinal tumours among Chinese and Malay patients was metastases, while the most common histological type of brain and spinal tumours among Indian patients and patients of other races was meningiomas.

Interventions and complications from surgery

The interventions administered and complications from surgery are presented in Table S4 [see Supplemental Digital Appendix]. It shows that 97.8% (490 patients) of patients had their tumour(s) resected, while 2.2% (11 patients) of patients received only stereotactic biopsy of the tumour with no subsequent resection. Among these 11 patients, three patients had glioblastoma, two patients had anaplastic astrocytoma and one patient each had diffuse midline glioma, low-grade infiltrating glioma (undefined histological subtype), diffuse large B-cell lymphoma (nongerminal centre subtype), metastatic bladder transitional cell carcinoma, metastatic breast carcinoma and metastatic prostate carcinoma. The reasons for not performing a resection after the initial stereotactic biopsy included difficult location of the tumour (6 patients), presence of too many lesions (3 patients), contralateral upper limb weakness after the initial stereotactic biopsy (1 patient) and increased perceived surgical risk due to the advanced age of the patient (1 patient).

Seventy-six (15.2%) patients received adjuvant gamma knife radiosurgery, 75 (15.0%) patients received adjuvant radiotherapy, 72 (14.4%) patients received adjuvant chemotherapy and 27 (5.4%) patients received adjuvant whole-brain radiotherapy. Among the 38 patients who had glioblastoma, 26 were treated with maximal safe resection followed by the Stupp protocol of concomitant radiotherapy and chemotherapy with temozolomide at our institution. Among the 12 patients with glioblastoma who were not treated according to the Stupp protocol at our institution, four patients declined treatment according to the Stupp protocol, three patients were not physically fit for radical radiotherapy, two patients were treated according to the Stupp protocol at another institution, and two patients who initially agreed to be treated according to the Stupp protocol were lost to follow-up and, therefore, did not start or complete the treatment. One patient was not offered treatment according to the Stupp protocol, as the patient had already been treated according to the Stupp protocol at another institution. Instead, this patient was treated with maximal safe resection and adjuvant pembrolizumab at our institution.

The most common complications after surgery were cerebrospinal fluid (CSF) leak (30 patients, 6.0%), diabetes insipidus (26 patients, 5.2%) and urinary tract infection (26 patients, 5.2%). Complications were the most common after surgery for tumours of the sellar region, with CSF leak (20 patients, 20.2%), diabetes insipidus (20 patients, 20.2%) and syndrome of inappropriate antidiuretic hormone (11 patients, 12.2%) being the three most common complications.

Time to all-cause mortality and recurrence

The Kaplan–Meier curves for all-cause mortality and recurrence of selected histological types of brain and spinal tumours are presented in Figures 1 and 2. High-grade gliomas and metastases had the poorest survival rates, with 180-day survival rates of 87.8% and 95.0%, respectively, and 1-year survival rates of 75.5% and 78.3%, respectively. The median overall survival of high-grade gliomas and metastases was 19.1 and 12.7 months, respectively. Among the high-grade gliomas, glioblastoma had the poorest prognosis, with a median overall survival of 16.5 months. High-grade gliomas and metastases also had the highest rates of tumour recurrence, with 180-day recurrence rates of 12.2% and 13.3%, respectively, and 1-year recurrence rates of 20.4% and 25.0%, respectively.

DISCUSSION

In our retrospective surgical cohort of 501 consecutive patients with brain or spinal tumours, the most common histological types were metastases (23.0%), meningiomas (22.0%) and

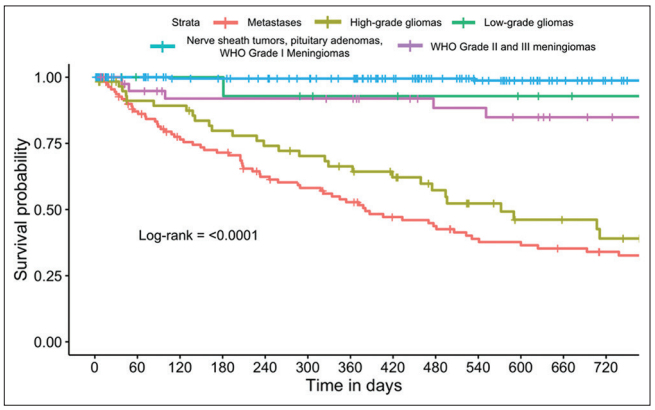

Figure 1: Kaplan–Meier curve for survival of selected histological types of central nervous system tumours. WHO: World Health Organization

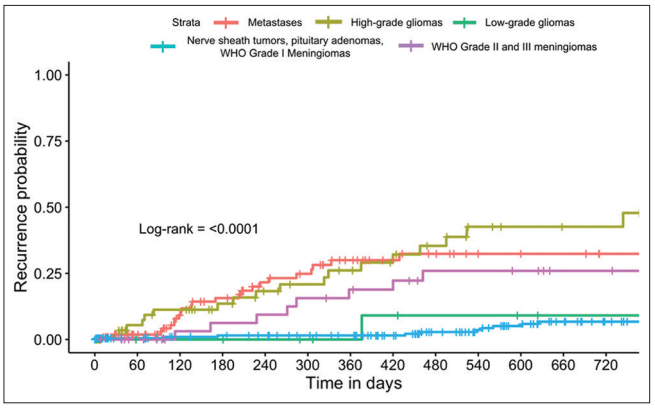

Figure 2: Kaplan–Meier curve for recurrence of selected histological types of central nervous system tumours. WHO: World Health Organization

tumours of the sellar region (18.0%). On the other hand, the most common histological types in the local study published in 2000 were meningiomas (35.1%), pituitary adenomas (11.8%) and metastases (10.0%).[8] The higher incidence of metastases may be related to improvements in detection of small metastases by magnetic resonance imaging (MRI) and improvements in cancer therapy since 2000.[10]

The incidence of metastases, meningiomas and tumours of the sellar region reported by other surgical cohorts internationally ranged from 4% to 12%, 21% to 26% and 1.8% to 22%, respectively.[11-14] The incidence of meningiomas and tumours of the sellar region at our institution falls within the range of the incidences reported by other surgical cohorts. However, our institution had a considerably higher incidence of metastases. The wide-ranging incidence of tumours of the sellar region reported in international surgical cohorts (1.8%–22%) is also worth noting.

Patients who had grade I or II gliomas tended to be younger, (mean age 29.0 and 40.5 years, respectively) compared to patients with other histological types of brain or spinal tumour (mean age 48.4–63.3 years). The mean age of patients with grade I or II gliomas in our cohort falls within that of other international surgical cohorts (21.9–39 years[15,16] and 33.6–47 years,[15-17] respectively).

In our cohort, there were more male patients who had tumours of the sellar region, gliomas, and mesenchymal, non-meningothelial tumours, while patients who had metastases, meningiomas, nerve sheath tumours and primary CNS lymphoma were mostly female. There was an equal distribution of male and female patients among patients who had other astrocytic tumours. Among the Chinese and Malay patients, the most common histological type was metastases, while the most common histological type among the Indian patients and patients of other races was meningiomas. Tumours of the spine were mostly benign, with the most common histological type being nerve sheath tumours. However, there were also a significant number of patients who had malignant tumours of the spine, with metastases being the second most common histological type of spinal tumour.

Common complications after surgery for brain and spinal tumours included surgical site haematoma,[18,19] with complication rates ranging from 1.1% to 3.2%,[20-22] and seizures,[18,19] with complication rates ranging from 4.6% to 37.0%.[23-26] In particular locations such as tumours of the sellar region, common surgical complications from resection of the sellar tumour included CSF leak, with complication rates ranging from 6% to 50%,[27-30] and diabetes insipidus, with complication rates ranging from 8.7% to 26.0%.[31-34] The incidence of postoperative surgical site haematoma, CSF leak and diabetes insipidus in our cohort fell within the international literature range, except for postoperative seizures, which was lower than that of the reported rates in the literature. This could be because at our institution, patients are routinely prescribed antiepileptics perioperatively.

With regards to survival outcomes, the median overall survival of glioblastoma in our cohort was 16.5 months. Other surgical cohorts reported median overall survival ranging from 11.0 to 15.9 months for glioblastoma.[7,35]

In conclusion, we provided a comprehensive update of the epidemiology of brain and spinal tumours managed surgically, which could help guide further studies on brain and spinal tumours in the future. However, our study involved only one institution, and hence may not be representative of the epidemiology of brain and spinal tumours in our country. Overall, the most common histological types of tumours in our cohort were metastases, meningiomas, tumours of the sellar region, nerve sheath tumours and high-grade gliomas. The most common histological types of brain and spine tumours were metastases and nerve sheath tumours, respectively. The most common presenting symptoms for brain tumours were cranial nerve palsy, headache and dizziness, while the most common presenting symptoms for spine tumours were weakness, numbness and back pain. The most common complications after surgery were CSF leak and diabetes insipidus, which were primarily from surgery for tumours of the sellar region. High-grade gliomas and metastases had the poorest survival and highest recurrence rates, and may therefore benefit from more specialised attention, such as from palliative care physicians, where indicated.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Supplemental digital content

Appendix at http://links.lww.com/SGMJ/A42

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