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Clinical commentary

Prognostic indicators of adult medullary gliomas after microsurgical treatment – A retrospective analysis of 54 patients

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ABSTRACT

Due to the low incidence of medullary gliomas, the special location, and the function of the gliomas in the medulla oblongata, microsurgical treatment is still challenging for neurosurgeons. The aim of this study was to observe the effect of microsurgical treatment of adult medullary gliomas and to explore the prognostic factors after treatment. The clinical data from 54 patients with adult medullary gliomas who received microsurgical treatment at Beijing Tiantan Hospital (China) from April 2008 to April 2014 was retrospectively analyzed. The factors affecting their prognosis were analyzed with log-rank univariate analysis. The factors that affected prognosis included age, gender, duration of preoperative symptoms, Karnofsky Performance Scale (KPS) score, World Health Organization (WHO) grade, extent of tumor resection, and postoperative complications. Those with statistical significance in the univariate analysis were entered into a multivariate Cox regression analysis. WHO grading showed 7 cases of grade I, 30 cases of grade II, 14 cases of grade III, and 3 cases of grade IV tumors. Univariable analysis showed that postoperative nasogastric feeding ($P = 0.031$), WHO pathological grade ($P = 0.018$), extent of resection ($P = 0.016$), and preoperative involvement of $\geq$3 cranial nerves (CNs) ($P = 0.014$) affected overall survival. The WHO pathological grade of the tumor was an independent risk factor for prognosis. In conclusion, the WHO pathological grade of the tumor was an important prognostic indicator.

1. Introduction

Adult brainstem gliomas comprise 1% of adult brain tumors and are the most common neoplasms involving the brainstem, with a median survival of 85 months (range, 1–228 months) [1,2]. Radiotherapy is the standard treatment for adult diffuse intrinsic brainstem gliomas and can improve or stabilize patients for years [3]. At present, the optimal timing for treatment remains unknown, and radiotherapy for brainstem gliomas is not satisfactory. The efficacy of chemotherapy in adult diffuse brainstem gliomas remains unproven, and adjuvant chemotherapy cannot be recommended [4]. There are no therapeutic targets nor targeted drug treatments for brainstem gliomas. The resection of diffuse intrinsic brainstem gliomas is impossible. In proposing the classification of "dorsally exophytic brainstem glioma", Hoffman has posited that surgical resection of tumors can prolong the survival of the patients [5]. Moreover, the surgical treatment of focal brainstem gliomas has been recognized elsewhere [6]. Brainstem gliomas mostly occur in the pons, whereas cases in the midbrain and medulla oblongata are relatively rare [7] and generally have a low pathological level (WHO grades I-II) [2]. In an analysis by Reithmeier et al., among 99 reported cases of adult brain stem glioma, six were limited to the medulla oblongata [8]. The medulla oblongata is a passageway for sensory and motor fibers and has many important internal nuclei and reticular structures that are involved in the reflex regulation of respiratory and cardiovascular functions [9,10]. Therefore, surgical resection of medullary gliomas is extremely challenging for neurosurgeons. This study included 54 cases of adult medullary gliomas and analyzed the clinical data, pathological characteristics, efficacy of microsurgery, and prognostic factors that influenced the postoperative survival of the patients. The aim of this study was to observe the effect of microsurgical treatment of adult medullary gliomas and to explore the prognostic factors after treatment. We hypothesized that certain factors, such as high-grade pathology, gross total resection of the tumor, tumors involvement of $\geq$3 CNs, and postoperative nasogastric feeding would be associated with poorer prognosis. The results showed that the WHO pathological grade of the tumor is an important prognostic indicator.

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2. Methods

2.1. Inclusion criteria

Included in the study were adult (age ≥16 years) patients with medullary gliomas who received microsurgical treatment between April 2008 and April 2014 in the brainstem ward of Beijing Tiantan Hospital. Preoperative MRIs of each patient showed that the tumor or the main body of the tumor was located in the medulla oblongata, with exogenous or endogenous focal growth that may have invaded the pons or cervical cord. The included patients did not receive any treatment before surgery and had no serious illness. The cases were pathologically diagnosed as gliomas and graded based on the World Health Organization (WHO) classification (2007) [11]. The patients agreed to participate in this study and to complete the follow-up interview; informed consent was provided.

2.2. Exclusion criteria

Patients were excluded from the study when postoperative treatment could not be completed following the normal medical procedure and the necessary treatment was skipped. Excluded cases also included those whose important clinical data were incomplete, as well as those cases in which the main bodies of the tumors involved the cerebellum, pons, and cervical cord with absence from the medulla.

2.3. Imaging data

All of the cases underwent brain MRI scans and enhanced scans. The tumor diameter varied within the range of 1.0–2.5 cm. Tumors were hypointense or isointense on T1-weighted images and were hyperintense on T2-weighted images. Some individual cases showed mixed signals, with hemorrhage, necrosis, or cystic degeneration along with obvious edema and mass effect surrounding the tumor. Thirty-seven tumors demonstrated enhancement. The tumors were classified as ventral type in 12 patients and dorsal type in 42 patients. With respect to the involvement of adjacent structures, the tumors were also classified as medullary type in 27 patients, pontomedullary type in 22 patients, and cervicomedullary type in five patients, with a clear boundary in 16 cases and no clear boundary in 38 cases. A postoperative brain CT scan was performed in 54 cases, and a postoperative (3–30 days) brain MRI scan was performed in 40 cases, with an average scan time of 9 days following surgery.

2.4. Treatment methods

Microsurgical treatment was performed in 54 patients. The patient was placed in a lateral or a lateral prone position. According to the location of the main body of the tumor and its growth pattern based on imaging, two surgical approaches were applied: a midline suboccipital approach in 39 patients and a far lateral suboccipital approach in 15 patients. All patients underwent surgery with real-time intraoperative neurophysiological monitoring. The early warning effect of brainstem auditory evoked potentials (BAEPs) and the brainstem mapping (BSM) technique were used to confirm the safe entry zones of the brain stem [12]. In some cases, surgery in the late stage was completed with neural navigation and diffusion tensor tractography (DTT). Postoperative radiotherapy was provided to 15 patients. The total prescription dose was 45–60 Gy, with 1.5–2.0 Gy/day administered 5 times/week for 6 weeks. Postoperative chemotherapy with oral temozolomide was provided in 3 cases.

2.5. Follow-up

The patients underwent follow-up at 3, 6, and 12 months. According to the pathological level with adjustments, the follow-up was mainly performed in the form of an outpatient review, with a telephone interview in some cases. The recorded contents included symptomatology, the Karnofsky Performance Scale (KPS), relapse in imaging, survival time, and cause of death.

2.6. Statistical methods

SPSS 19.0 statistical software was used for statistical processing. Overall survival (OS) was calculated using the Kaplan-Meier method. Univariate analysis was performed with the log-rank test. Multivariate analysis was performed using the Cox regression model to identify independent risk factors. A likelihood of $P < 0.05$ was considered to be statistically significant. The starting point for the observations was the operation date, whereas the endpoint event was death for the patients experiencing tumor recurrence. OS time was the survival time (in months) after the surgery.

3. Results

3.1. Patient population and clinical features

The demographics, pathological diagnoses, and clinical features for the 54 eligible patients are shown in Tables 1 and 2. There were 36 males and 18 females. The patients ranged in age from 16 to

Table 1
Characteristics of the 54 adult medullary gliomas.

Patient characteristics	
Age (years)	
Mean ± SD	35.6 ± 12.0
Median/range	38/(16–61)
Male/female	36/18
Median duration of symptoms (months)	3/(1–36)
Median KPS	80/(60–100)
Median F/U (months)	24/(3–96)
Median survival (months)	53/(1–96)
1-, 3-, 5-year survival rate (%)	87.9, 50.3, 46.4
Histopathology (n)	
WHO grade I/II/III/IV	7/30/14/3
Ganglioglioma	4
Pilocytic astrocytoma	2
Papillary glioneuronal tumor	1
Astrocytoma	25
Oligodendroglioma	5
Anaplastic astrocytoma	9
Anaplastic oligodendroglioma	5
Glioblastoma	3

KPS = Karnofsky Performance Sale, WHO = World Health Organization, F/U = follow-up.

Table 2
Symptoms of the 54 patients with adult medullary gliomas.

Patient characteristics	N (%)
Symptoms	
Dysdipsia	22 (40.7)
Dizziness	20 (37.0)
Hoarseness	14 (25.9)
Gait disturbance	13 (24.0)
Sensory symptoms	10 (18.5)
Limb weakness	8 (14.8)
Vomiting	6 (11.1)
Dyspnea	2 (3.7)