Original Article

Diagnosis and outcomes of pediatric central nervous system tumors in China: a single-center retrospective analysis from 2015 to 2020

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Background: A primary central nervous system (CNS) tumor is the most common solid tumor among children, but few systematic and comprehensive studies on childhood CNS tumors in China. We aim to review the characteristics, treatments, and prognosis of childhood CNS tumors in a single-center and disclose the present issues on these tumors.

Methods: The cross-sectional retrospective study analyzed patients with primary CNS tumors who were under 18 years old at Zhujiang Hospital, Southern Medical University (Guangzhou, China), from 2015 to 2020. Demographics, tumor types, localizations, histological characteristics, treatment strategies, and outcomes were assessed. Data were performed in descriptive statistics (means, ranges and 95% confidence intervals), and survival analysis was estimated based on the Kaplan-Meier method using SPSS Statistics 21.0 (IBM Corp., Armonk, NY, USA).

Results: There were 445 patients screened and 431 patients enrolled in this study. The median age was 7 years old (ranging from 14 days to 18 years old), and the male to female ratio was 1.71 (272:159). The locations of CNS tumors consisted of supratentorial (n=261, 60.56%), infratentorial (n=143, 33.18%), and spinal cord (n=27, 6.26%). The major types of CNS tumors were glioma (n=102), medulloblastoma (n=57), hemangioma (n=34), ependymoma (n=30), nongerminomatous germ cell tumors (n=27), germinoma (n=24), and craniopharyngioma (n=14). The rate of surgery was 83.99% (n=362) and that of radiotherapy/chemotherapy alone was 4.64% (n=20). Seventy-five patients (17.40%) discontinued or refused parts of their treatment, and 49 patients (11.37%) abandoned treatments on tumor. There were 308 patients (71.46%) alive, 82 (19.03%) dead, and 41 patients (9.51%) who were not available for follow-up by the end of the study. The 5-year survival rate of low-grade glioma (LGG), medulloblastoma, other embryonal tumors, ependymoma (World Health Organization grade III), germinoma, nongerminomatous germ cell tumors was 82.7%, 56.5%, 58.4%, 73.8%, 100.0%, and 53.8%, respectively. The 3-year survival rate of high-grade glioma (HGG) and ependymoma (World Health Organization grade I–II) was 22.0% and 82.1%, respectively.

Conclusions: The study partly reflected the current situation of Chinese children with CNS tumors from

a tertiary hospital. The high proportion of treatment refusal and abandonment, and the poor outcomes of patients with CNS tumors, show that it need more effort to improve the prognosis in the future.

Keywords: Central nervous system tumors; pediatric; China; prognosis; abandoned treatment

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Introduction

Central nervous system (CNS) tumors refer to a group of benign and malignant diseases originating from tissues or structures in the central nervous system. The primary CNS malignant tumor is the second most common malignant tumor and the most common solid tumor among children (1). There were 330,000 cases of CNS tumors and 227,000 related deaths worldwide between 1990 and 2016, with the highest incidence in the regions East Asia, Western Europe, and South Asia, and the countries China, the United States, and India. The incidence of CNS tumors peaked in early childhood (<5 years old) and increased after the age of 15 years old (2). China is a developing country with the largest population globally and many pediatric patients with neurological neoplasms (3). Glioma was the most common CNS tumor in high-income countries, followed by embryonal tumors (4). In low- and middle-income countries, a study carried out by the largest children's cancer hospital in the Middle East found that the most common histological types of CNS tumors were astrocytoma, embryonal tumors, ependymoma, and craniopharyngioma (5). In China, research on children under two or three years old found that astrocytoma was the most common tumor type, followed by ependymoma or medulloblastoma (MB) (6,7). These studies partially demonstrated the incidence, histological types, and distributions of childhood CNS tumors in China, but did not contain a systematic and detailed report on these.

The prognosis of childhood CNS tumors has not improved significantly in Europe and the United States in the past 10 years, and the 5-year survival rate has remained at between 56.7% and 58.2% in Europe (8), 63% in the United States (9), 59% in South Korea (10), and about 60% in Japan (11). Furthermore, the 5-year survival rate was low in areas with less developed economic and medical conditions, such as 46.4% in South Africa and 27.0% in India (12,13). Compared to low-grade glioma (LGG), high-grade glioma (HGG), primitive neuroectodermal tumor (PNET), and MB had an increased risk of mortality. Brainstem and cerebrum tumors also had a greater risk of mortality than tumors in lobes (14). Although the survival rates of malignant childhood CNS tumors have improved with advances in surgical and adjuvant therapies, unfortunately, the prognoses for patients with tumors such as diffuse intrinsic pontine glioma (DIPG) and tumors with metastasis at diagnosis remain poor, significantly affecting the qualities of patients' life and leading to the higher mortality rates (15).

Compared with other kinds of cancers in children, the rate of abandoning treatments in patients with CNS tumors is higher because of complexity of the disease, increased medical costs, and long-term treatment procedure (16). Multidisciplinary management is significant for children with CNS tumors during standard treatment and improving their prognosis (17), which may reduce the gap in the clinical management of CNS tumors in middle-income countries (18).

Since 2013, basic health medical insurance has achieved nearly universal coverage of the population in China (19). Like basic health insurance, critical illness insurance is an institutional arrangement to reimburse high medical expenses associated with a critical illness (20). The abandonment rate of treatment for leukemia has dropped from 50% to 10% due to the significant improvement of social health insurance schemes in China (21). However, the CNS tumors treatment abandonment rate is still high because of the increased economic burden, and ways to improve the medical insurance system to reduce the abandonment rate remain unclear (22).

Currently, there is also a lack of detailed information about the types and treatment outcomes of CNS tumors in children. In this paper, we review the characteristics, diagnosis, treatments and outcomes of childhood CNS tumors, especially for several typical tumors and provide databases for future research about childhood CNS tumors in China. We present the following article in accordance with the STROBE reporting checklist (available at https://

pm.amegroups.com/article/view/10.21037/pm-21-67/rc).

Methods

Patients and classification

Data on patients under 18 years old with CNS tumors were collected from January 1, 2015, to December 30, 2020, at Zhujiang Hospital, Southern Medical University in China. The last follow-up time was March 29, 2021. The search diagnostic code for this study followed the International Classification of Childhood Cancer-3 (ICCC-3) based on the International Classification of Diseases for Oncology (ICD) codes published in 2005 (23). Some rare tumors, such as atypical teratoid/rhabdoid tumor (AT/RT) and PNET, which are similar to MB, were classified as other embryonal tumors. The inclusion criteria is that patients who received treatments related to CNS tumors like surgery, chemotherapy, radiotherapy and others in Zhujiang Hospital, and the exclusion criteria consists of only a diagnostic imaging without treatments or receiving treatments unrelated to CNS tumors, such as pneumonia, traumatic injury, and so on. Some patients diagnosed with MB or glioma performed molecular profiling by mutational and chromosomal copy-number variant analysis (n=6), NanoString (n=8), and clinical whole-exome sequencing (n=20) (24,25). The current consensus agrees upon four distinct molecular subgroups in MB, including wingless-activated (WNT), sonic-hedgehog-activated (SHH), and Group 3 and Group 4 (26).

Gender, age, primary tumor location, histology, treatment, and survival data were collected for each patient. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the Institutional Review Board (IRB) of Zhujiang Hospital, Southern Medical University (ID: 2021-KY-069-01). According to applicable laws and regulations, a waiver of informed consent was approved by the IRB of Zhujiang Hospital.

The diagnosis of CNS tumors was based on pathologies, imaging features, and serum/cerebrospinal fluid (CSF) tumor markers like Alpha-fetoprotein (AFP) and β-human chorionic gonadotropin (β-hCG). The diagnostic criteria of tumor markers for germinoma (GCT) (β-hCG 3–50 mIU/mL and/or AFP 0–25 μg/L) and nongerminomatous germ cell tumors (NGGCT) (β-hCG ≥50 mIU/mL and/or AFP ≥25 μg/L) was applied when in the absence of a pathology examination or CSF cytology (27).

Treatment

The standard clinical treatments for MB, ependymoma (World Health Organization (WHO) grade III), and HGG are surgery, radiotherapy, and chemotherapy for patients over three years old and the same but without radiotherapy for patients under three years old. The primary treatments for LGG and other WHO grade I–II tumors are a complete resection, and radiotherapy and/or chemotherapy can be applied for patients with unresectable or residual masses. The chemotherapy protocol for MB is CCCG-MB-2017 (28). The chemotherapy agents for LGG are carboplatin and vincristine (29), which combine vemurafenib for patients with the BRAF-V600E mutation (30). The treatment agents for HGG contain temozolomide, semustine, vincristine, carboplatin/cisplatin, etoposide, and bevacizumab for patients with progression or recurrence (31,32). The treatment agents for ependymoma contain vincristine, cyclophosphamide, carboplatin, etoposide, and methotrexate (33,34).

The standard treatments for GCT and NGGCT are chemotherapy and radiotherapy (for patients >3 years old). However, patients with residual tumors after chemotherapy and/or radiotherapy or with an uncertain diagnosis need to receive surgery or a biopsy. The chemotherapy regimens for GCT and NGGCT contain cyclophosphamide, ifosfamide, etoposide, cisplatin, and carboplatin (35).

Our multidisciplinary team (MDT) formed by pediatric neurosurgeons in 2019 consisted of radiotherapists, diagnostic radiologists, pathologists, and pediatric oncologists. The MDT discussed cases in detail on a weekly basis to agree on the best treatment protocol for each patient.

Critical illness insurance in Guangdong Province reimbursed patients for up to 60% medical costs, such as surgery, magnetic resonance imaging, chemotherapy, radiotherapy and others. However, patients and their families had to pay for some additional items like molecular profiling analysis out of their pocket.

Statistical methods

This study is a cross-sectional retrospective analysis, and the date of diagnosis was the time of resection/biopsy, imaging, and the tumor marker tests for any patients without a histological diagnosis. Descriptive statistics [means, ranges, and confidence intervals (CI) of 95%] were used to summarize the data. Overall survival (OS) was calculated as the time from diagnosis to either death of any cause or

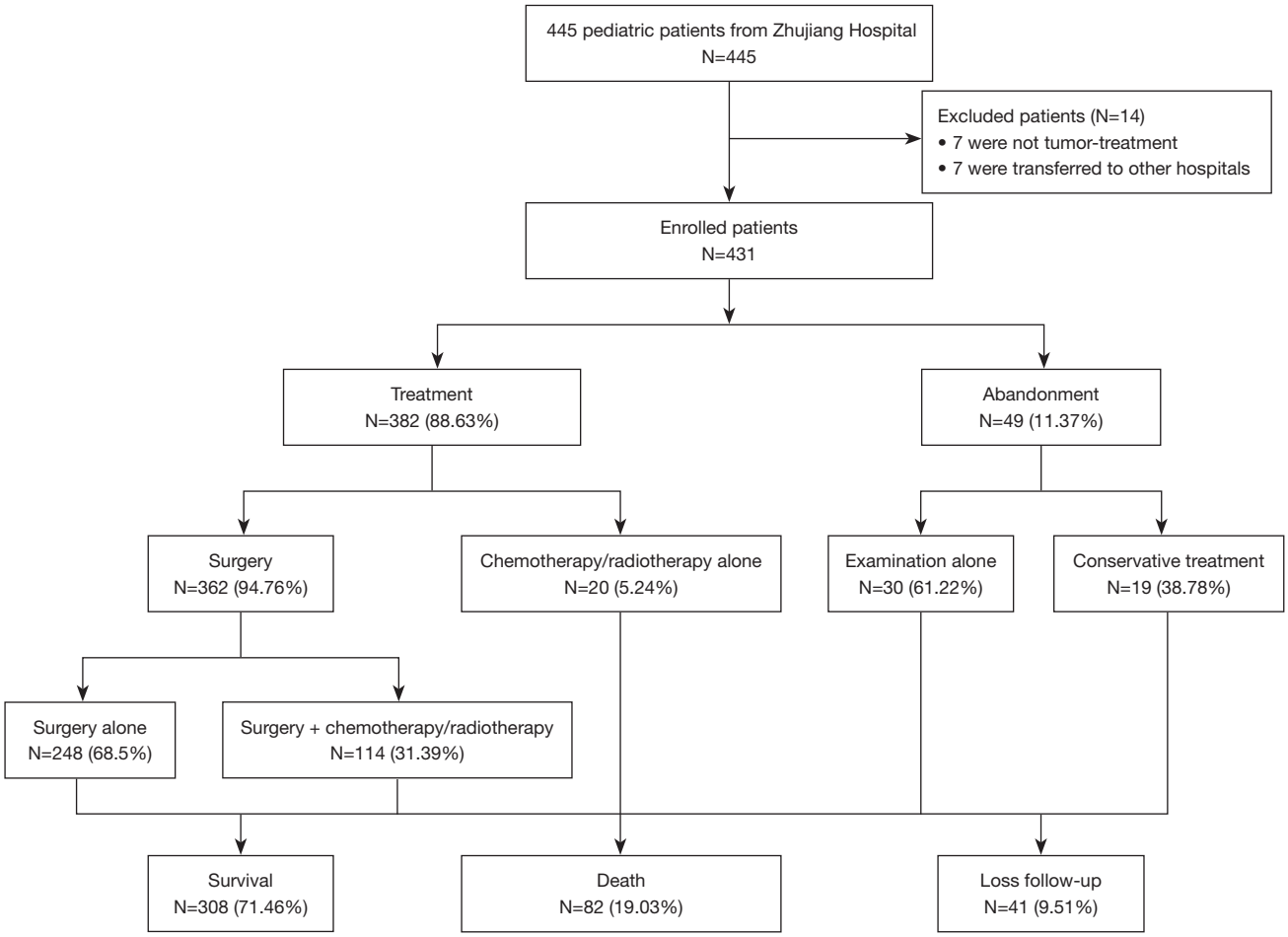

Figure 1 Study flow of patients.

the last follow-up. The probabilities of OS were calculated using the Kaplan-Meier estimator. Statistical analysis was performed with the SPSS Statistics 21.0 (IBM Corp., Armonk, NY, USA).

Results

The center received 445 pediatric patients with CNS tumors in the past six years. Up to 90% of patients were referred to our hospital from secondary hospitals without the ability to perform neurosurgery. There were 14 patients excluded in this study, including 7 patients diagnosed with imaging alone and transferred to other hospitals and 7 patients with treatments unrelated to tumors. Four hundred and thirty one patients were enrolled, including 22 patients who received surgery in our hospital and went to other hospitals for radiotherapy and/or chemotherapy (*Figure 1*). The newly diagnosed cases of CNS tumors in 2015, 2016, 2017, 2018, 2019, and 2020 were 61, 63, 56, 63, 96, and 92, respectively. The median age was 7 years old (ranging from 14 days to 18 years old), and the male to female ratio was 1.71 (272:159) (*Figure 2*). The locations of CNS tumor consisted of supratentorial (n=261, 60.56%), infratentorial (n=143, 33.18%), and the spinal cord (n=27, 6.26%) (*Figure 3*). The tumor types were various, including glioma (n=102, 26.70%), MB (n=57, 14.92%), NGGCT (n=27, 7.07%), GCT (n=24, 6.28%), hemangioma (n=34, 8.90%), ependymoma (n=30, 7.85%), and craniopharyngioma (n=14, 3.66%), etc. (*Figure 4*). The data of 6 cases were presented in the MDT meeting in 2019, and 65 cases in 2020.

There were 362 patients (83.99%) who had a surgical resection or biopsy, and 20 patients (4.64%) who underwent radiotherapy or chemotherapy alone. The rest of the patients (n=49) refused or abandoned treatment,

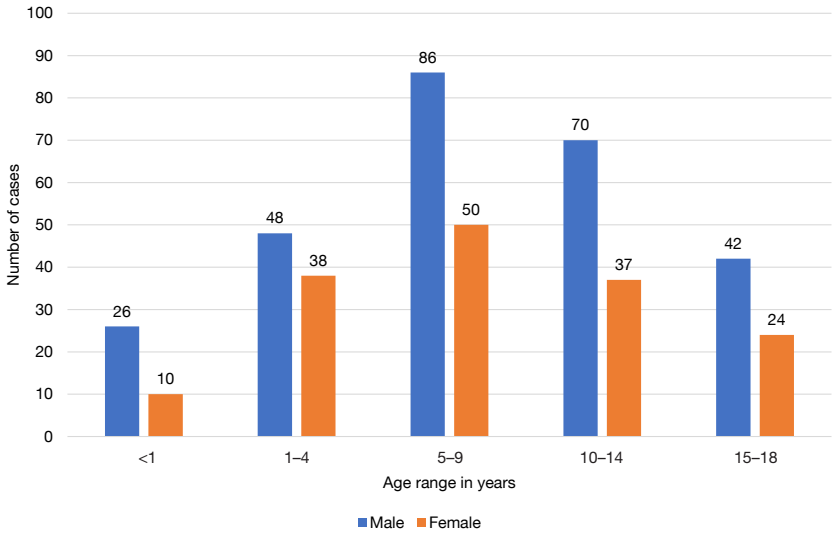

Figure 2 Distribution of sex and age in childhood central nervous system tumors.

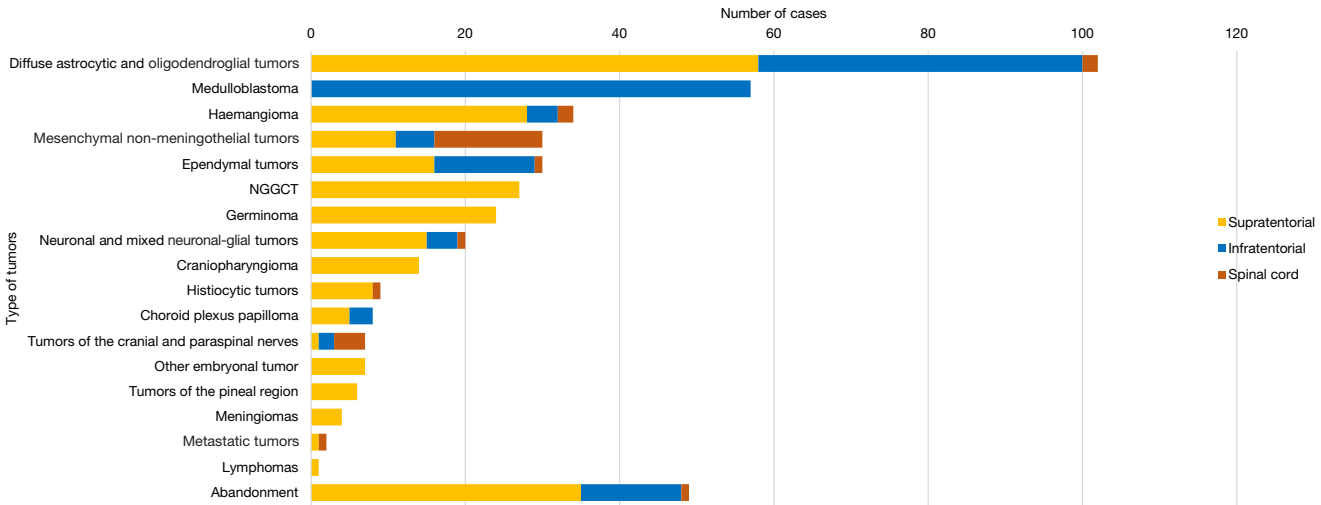

Figure 3 Location of childhood central nervous system tumors. NGGCTs, nongerminomatous germ cell tumors.

and they only received an examination (n=30, 6.96%) and conservative treatments (n=19, 4.41%) such as ventriculoperitoneal shunts or Ommaya reservoir insertion to relieve intracranial pressure or hydrocephalus, and anti-epileptic or anti-inflammatory treatments. There were 308 patients (71.46%) who survived, 82 (19.03%) who died, and 41 (19.51%) who were not available for the follow-up because they refused to answer the telephone or the telephone number provided in this study no longer functioned (*Figure 1*).

Glioma

LGG (n=79) was the most common glioma in this study. The median age of patients with LGG was 7 years old (ranging from 3 months to 18 years old), and the male-to-female ratio was 1.26 (44:35) (*Table 1*). Seven patients had performed clinical whole-exome sequencing (WES) analysis, 2 had the PIK3CA mutation, 2 had the BRAFp. V600E mutation, and 3 had BARF-KIAA1549 fusion. Sixty-six patients underwent a complete resection, 2 patients underwent a biopsy, and 11 patients had a subtotal

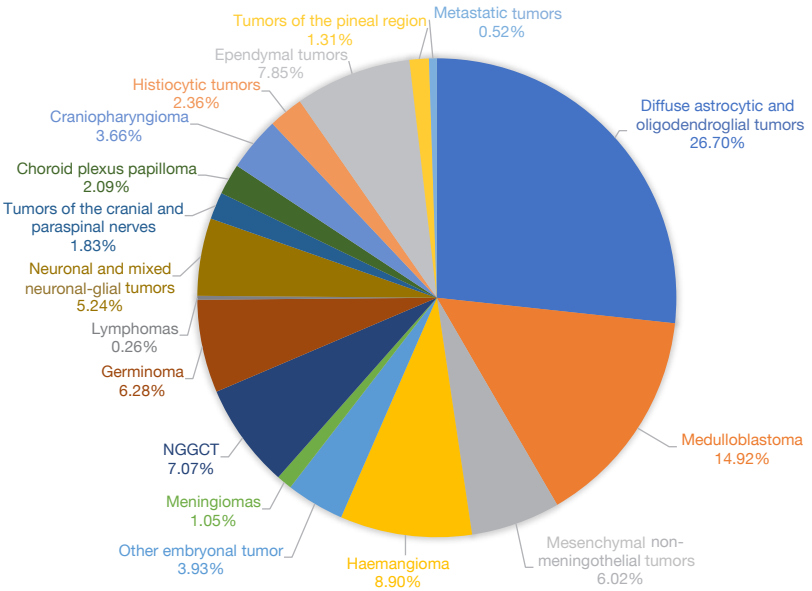

Figure 4 Types of childhood central nervous system tumors. Diffuse astrocytic and oligodendroglial tumors: astrocytomas (n=91); oligodendrogliomas (n=11). Mesenchymal, non-meningothelial tumors (haemangioma excluded): haemangioblastoma (n=3); chondrosarcoma/osteoblastoma/osteoma (n=4); lipoma (n=13); haemangiopericytoma/solitary fibrous tumor (n=1); chordomas (n=2). Other embryonal tumors: atypical teratoid/rhabdoid tumor (n=3), neuroblastoma (n=1); ependymoblastoma (n=2); medulloepithelioma (n=1); Ewing sarcoma (n=7); pineoblastoma (n=1). NGGCTs (n=27); neuronal and mixed neuronal-glial tumors: mixed neuronal-glial tumors (n=2); ganglioglioma (n=6); central neurocytoma (n=3); desmoplastic infantile astrocytoma and ganglioglioma (n=1); gangliocytoma (n=2); dysembryoplastic neuroepithelial tumor (n=5); diffuse leptomeningeal glioneuronal tumor (n=1). Tumors of the cranial and paraspinal nerves: neurofibroma (n=2); hybrid nerve sheath tumors (n=5). Histiocytic tumors: langerhans cell histiocytosis (n=9). Tumors of the pineal region: pituicytoma (n=5). Metastatic tumors: myeloid sarcoma (n=1); neuroblastoma (n=1). NGGCTs, nongerminomatous germ cell tumors.

resection, including 4 patients who had radiotherapy and/or chemotherapy. Eight patients discontinued treatments, including 6 underwent a subtotal resection. The median follow-up period for LGG was 27.61 months, and OS was 64.74 months, with a 5-year OS rate of 82.7% (*Figure 5*).

There were 6 cases of optic pathway glioma, including 1 patient with neurofibromatosis 1 (NF1) who was treated with a subtotal resection and chemotherapy. Among the 2 cases with the BRAFp.V600E mutation, one patient was treated with vemurafenib combined with chemotherapy and the other was treated with vemurafenib alone after chemotherapy; however, the tumor size of both patients had shrunk, but the impaired vision could not be restored.

There were 23 patients with HGG, and the median age was 11 years old (ranging from 4 months to 18 years old), with the male to female ratio of 1.56 (14:9). Two cases had tumor molecular profiling analysis, 1 case had the H3F3A p. K28M mutation. The other case had the IDH1 mutation (p. R132H c. 395G > A) and MSH6 germline mutation without a family history. Of 23 patients who underwent surgery, 5 patients received chemoradiotherapy, and 1 patient under 3 years old received chemotherapy. A total of 16 patients discontinued treatments during the course of the study, because they died post-surgery before initiation of chemoradiotherapy (n=2), they were in a coma and vegetative state after surgery (n=2), they had hydrocephalus (n=1), they continued treatment with traditional Chinese Medicine (n=1), or because of personal or financial reasons (n=10). The median follow-up period and OS of HGG was 9.83 months and 19.17 months, respectively, with a 3-year OS rate of 22.0%.

There were 24 brain stem tumor patients, with the median age of 8 years old (ranging from 3 to 13 years old), and the male-female ratio was 1.18 (13:11) (*Table 2*). Of 10 patients with DIPG, 5 were pathological diagnoses (3 LGG patients and 2 HGG patients), and 5 were identified by diagnostic imaging. There were 5 patients who underwent a surgical biopsy, but only 1 patient received chemoradiotherapy. None of the patients underwent molecular profiling analysis. The median follow-up period

Table 1 Demographics and clinical management of patients with different types of central nervous system tumors

Tumor types	Total	Age (years), mean (range)	Sex (M/F)	Surgery, n (%)	RT, n (%)	CT, n (%)	Discontinued/ refused treatment, n (%)	Recurrence	Median follow-up period (Mos.) (95% CI)	OS (Mos.) (95% CI)
MB	57	7 [1, 17]	2.0	57 (100.0)	31 (54.4)	35 (61.4)	21 (36.8)	17 (29.8)	19.98 (15.73, 24.89)	46.93 (37.32, 56.55)
Other embryonal tumors[a]	15	5 (3 Mos, 14)	1.1	15 (100.0)	3 (20.0)	5 (33.3)	9 (60.0)	5 (33.3)	21.80 (13.40, 32.19)	48.36 (30.91, 65.80)
Ependymoma (WHO grade I–II)	13	4 [1, 18]	0.86	13 (100.0)	1 (7.7)	2 (15.4)	0 (0.0)	1 (7.69)	19.46 (11.00, 29.29)	47.15 (35.97, 58.34)
Ependymoma (WHO grade III)	17	5 (5 Mos, 17)	3.25	17 (100.0)	6 (35.3)	7 (41.2)	8 (47.06)	6 (35.3)	33.35 (22.86, 44.66)	58.19 (46.50, 69.88)
LGG	79	7 (3 Mos, 18)	1.26	79 (100.0)	9 (11.4)	13 (16.5)	8 (10.12)	7 (8.9)	27.61 (22.96, 32.21)	64.74 (59.06, 70.42)
HGG	23	11 (4 Mos, 18)	1.56	23 (100.0)	6 (26.1)	9 (39.1)	16 (69.57)	9 (39.1)	9.83 (5.26, 15.51)	19.17 (9.58, 28.75)
GCT	24	11 [2, 18]	2.43	14 (58.3)	19 (79.2)	21 (87.5)	6 (20.8)	1 (4.2)	25.92 (17.50, 35.50)	–
NGGCTs	27	9 (14 days, 16)	2.38	20 (74.1)	13 (48.1)	21 (77.8)	7 (25.93)	7 (25.9)	25.85 (19.93, 31.63)	52.11 (43.39, 60.82)

[a], medulloepithelioma (n=1); atypical teratoid/rhabdoid tumor (AT/RT) (n=3); CNS neuroblastoma (n=1); ependymoblastoma (n=2); ewing sarcoma/ PNET (n=7); pineoblastoma (n=1). M/F, the ratio of male and female; RT, radiotherapy; CT, chemotherapy; Mos, months; CI, coincidence interval; OS, overall survival; MB, medulloblastoma; LGG, low-grade glioma; HGG, high-grade glioma; GCT, germinoma; NGGCTs, nongerminomatous germ cell tumors.

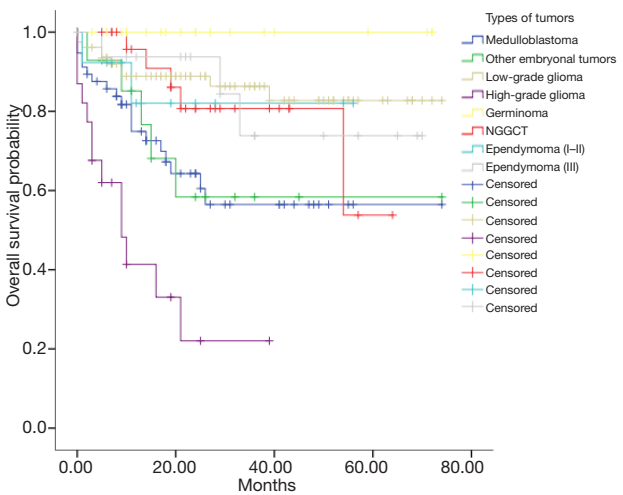

Figure 5 Overall survival of childhood central nervous system tumors. WHO, World Health Organization; NGGCTs, nongerminomatous germ cell tumors.

was half a month, and OS was 4.32 months with a 3-year OS rate of 27.3%.

Embryonal tumors

Embryonal tumors were the second most common CNS tumors, and MB (14.92%) was the major type of embryonal tumors. The median age was 7 years old (ranging from 1 to 17 years old), and the ratio of male to female was 2.0 (48:24). The histologic subtypes of MB were mainly classic (n=31) and Desmoplastic/nodular (n=26). Molecular classification of MBs had been performed in 25 patients, including 1 patient belonging to WNT, 6 to SHH, 4 to Group 3, and 14 to Group 4. The reasons for discontinued treatments in 21 patients were postoperative infection (n=6), hydrocephalus (n=4), cerebellar mutism (n=2), tumor progression (n=2), brain herniation (n=1), continuing treatment with traditional Chinese medicine (n=1), and personal and economic reasons (n=5). The median follow-up period was 19.98 months, and OS was 46.93 months, with an OS rate of 56.5%. The other embryonal tumors were AT/RT (n=3), central neuroblastoma (n=1), ependymoblastoma (n=2), medulloepithelioma (n=1), PNET (n=7), and pineoblastoma (n=1). Nine patients discontinued treatments because they died after postoperative complications (n=3), they had

Table 2 Characteristics of brain stem gliomas

Clinical characteristics	Non DIPG, n (%)	DIPG, n (%)
Total	14	10
Age, years [range]	8 [3, 13]	8 [5, 10]
Sex		
Male	10 (71.40)	3 (30.00)
Female	4 (28.60)	7 (70.00)
Histologic		
LGG	3 (21.43)	3 (30.00)
HGG	1 (7.14)	2 (20.00)
Hemangioma	4 (28.57)	0 (0.00)
Unknown	6 (42.85)	5 (50.00)
Treatment		
Surgery alone	8 (57.14)	4 (40.00)
ST + RT + CT	0 (0.00)	1 (10.00)
Untreated	6 (42.86)	5 (50.00)
Median follow-up period (Mos) (95% CI)	4.00 (0.00, 20.00)	0.50 (0.00, 10.00)
OS (Mos)	47.10 (24.50, 69.69)	4.32 (1.32, 7.32)

CI, coincidence interval; Mos, months; DIPG, diffuse intrinsic pontine glioma; LGG, low-grade glioma; HGG, high-grade glioma; ST, surgery; RT, radiotherapy; CT, chemotherapy; OS, overall survival.

an infection (n=1), they had hydrocephalus after surgery (n=1), they continued treatments with traditional Chinese medicine (n=1), and for personal or financial reasons (n=3). The median follow-up period was 21.80 months, and OS was 48.36 months, with an OS rate of 58.4%.

Ependymoma

There were 13 patients with WHO grade I/II ependymoma, and the median age was 4 years old (ranging from 1 to 18 years old), with the male-to-female ratio of 0.86 (6:7). All patients received surgery, and 1 patient had a recurrence. The mean follow-up period was 19.46 months, and OS was 58.19 months, with a 3-year OS rate of 82.1%.

Seventeen patients had ependymoma (WHO grade III), and the mean age was 5 years old (ranging from 5 months to 17 years old), with the male to female ratio of 3.25 (13:4). The causes of refused treatments in 8 patients were postoperative infection (n=2), secondary epilepsy (n=2), central paralysis (n=1), tumor progression (n=1), and economic and personal reasons (n=2). The mean follow-up time was 33.35 months, and OS was 58.19 months, with a 5-year OS rate of 73.8%.

Germ cell tumors

In 24 GCT patients, the median age of patients with GCT was 11 years old (ranging from 2 to 18 years old), with the male-to-female ratio of 2.43 (17:7). Ten patients were diagnosed with specific imaging features combined with negative tumor markers such as AFP and β-hCG, while 14 were pathological diagnoses. A total of 17 patients received chemoradiotherapy, and 1 patient under 3 years old was treated with chemotherapy. Treatment refusal in 6 patients was due to post-chemotherapy remission (n=1), chemotherapy complications (n=1), and personal and economic reasons (n=4). The mean follow-up period was 25.92 months and the 5-year OS rate was100%.

The median age of NGGCT was 9 years old (ranging from 14 days to 16 years old), and the male-to-female ratio was 2.38 (19:8). Among the 27 patients, 20 patients were confirmed by the pathological diagnoses, and 7 were diagnosed with elevated levels of tumor markers like AFP or β-hCG. AFP levels varied from 1.80 to 122,580.00 μg/L (median of 176.15 μg/L) in serum and from 0.90 to 1,605.00 μg/L (median of 22.60 μg/L) in CSF. β-hCG levels ranged from 0.20 to 3,833.00 mIU/mL (median of 6.67 mIU/mL) in serum and 0.63 to 527.79 mIU/mL (median of 68.34 mIU/mL) in CSF. There were 5 patients with high AFP serum levels up to 1,000 μg/L, of whom 1 patient developed tumor recurrence and 1 patient died from tumor progression. Seven patients discontinued treatments because they were in a coma after surgery (n=1), tumor progression under chemotherapy (n=1), and for personal and economic reasons (n=4). The mean follow-up period was 25.85 months, and OS was 52.11 months, with a 5-year survival rate of 53.8%.

Abandonment

In the initial consultation, 49 patients gave up treatments, even though the health insurance coverage rate was up to 91.83%. The median age was 6 years old (ranging from 4 months to 18 years old), and the male-to-female ratio was 2.5 (35:14). The main distributions of tumor locations were supratentorial (44.89%), infratentorial (24.89%), brain stem (28.57%), and spinal cord (2.04%). The 19 patients underwent conservative treatments, of whom

11 patients had received ventriculoperitoneal shunts (n=9) and Ommaya reservoir (n=2) to relieve intracranial pressure. Patients abandoned treatments because they had incorrect information about the disease, continued treatments with traditional Chinese medicine, or for family economic reasons and transportation issues.

Discussion

There are few publications about the incidence, treatments, outcomes, and follow-up in childhood CNS tumors in China (36). Tumors incidence, treatment strategies, and prognoses are various in races and regions (37). Patients with tumor dissemination, metastasis, and brain stem tumors abandoned treatments at the time of diagnosis in secondary medical facilities, and most of them did not transfer to tertiary hospitals for better treatments. This may be one of the reasons why the typical age onset and CNS tumors incidence in our center were slightly different from that of international reports, but the common types of CNS tumors are similar to previous reports like glioma, MB, and ependymoma (38,39). The incidence of NGGCT and pure germ cell tumors in the Asian population was higher than that in the European and American populations from 1987 to 2011 (40,41). The conclusions from most of these studies have shown a statistically significant increase in incidence of childhood CNS in China annually and a non-significant decrease in mortality (42). The National Brain Tumor Registry of China (NBTRC) is a registry of real-world clinical data on brain tumors that systematically collects data on patients with brain tumors in China. It was established in 2019 and has conducted database collection from February 1, 2019, to provide reliable clinical brain tumor data and perform specific nationwide multicenter clinical research (43).

Molecular diagnostic techniques for CNS tumors have been available in Beijing and Shanghai, and some consensus on classification of tumor molecular subtypes like MB. Some MB and glioma patients in our center have performed molecular profiling, but the relationship between molecular types and disease prognosis is unclear because of the limited cases. Targeted therapies (NCT04832672, NCT02672241), and immunological therapies (NCT04749641, NCT03914768, NCT02992210) have been carried out in some medical centers, which may promote the prognoses of CNS tumors in China. At present, patients in our center have not been enrolled in any clinical trials of molecular targeted or immunological therapies.

The prognoses (survival gap) of patients with pediatric CNS tumors in low-and middle-income countries is significantly worse than that in high-income countries (16), and our study also supports this point. The number of CNS tumors patients with tumors recurrences, progression, death and abandonment of treatments is still high in China, and treatment patterns can be a powerful prognostic factor in improving the outcomes of childhood CNS tumors in developing countries (44,45). In this study, nearly half of the patients with MB were treated by surgery alone, which was similar to previous studies in Shanghai (42). Previous research has reported that arsenic trioxide is effective in SHH-MB in preclinical studies, and patients in China may benefit from arsenic trioxide treatment (46,47). Previous studies found that high AFP level up to 1,000 ng/mL in serum or CSF indicated a poor prognosis (48), and 2 patients with tumor recurrence in our study which may correlate to short-time follow-up. The majority of HGG patients underwent surgery, but very few patients received surgery combined with chemoradiotherapy. At present, because most families regard childhood CNS tumors with lower survival rates and severe complications, they usually decide to give up subsequent radiotherapy and/or chemotherapy after surgery even though multidisciplinary management has been implemented in China.

There was a high treatment abandonment rate in CNS tumors because of the lack of financial support, transportation difficulties, delayed diagnosis, and neurological sequelae after surgery, among other factors. The imbalanced economic development in different regions of China also results in an uneven distribution of medical resources and different treatment protocols, leading to different final prognoses of patients with CNS tumors (22). Receiving an early diagnosis, applying standardized treatments, reducing the economic burden, helping parents realize the importance of chemoradiotherapy, and improving nursing quality will significantly contribute to childhood CNS tumors in the future (49).

The data in this study displayed the present treatment status and existing problems of the most common CNS tumors in Chinese children. However, our data were based on a single tertiary center in China and may not entirely exhibit the profile of whole communities. The data also could not reflect the relationship between treatments and prognoses because of limited CNS tumors types and a short follow-up time. The increasing incidence rate and low 3-year survival rate suggest that more efforts for prevention and intervention shall be needed in China to improve

outcomes of patients with CNS tumors (37,42,50).

Conclusions

The study showed the demographics, tumor locations, diagnosis, treatments, and outcomes of CNS tumors in children in China. It reflects the current issues of CNS tumors in Chinese children, such as discontinuation and abandonment of treatments, and provides future improvement and efforts to promote the survival.

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