Epidemiology, Clinical Presentation, and Prognosis of Pediatric Brain Tumors: Experience of National Center for Children's Health

wei yang (dr.yangwei@foxmail.com)
Beijing Children's Hospital Capital Medical University https://orcid.org/0000-0003-3157-6662

Yingjie Cai
National Center for Children's Health: Beijing Children's Hospital

Jiashu Chen
National Center for Children's Health: Beijing Children's Hospital

Ping Yang
National Center for Children's Health: Beijing Children's Hospital

Zesheng Ying
National Center for Children's Health: Beijing Children's Hospital

Yuting Liang
National Center for Children's Health: Beijing Children's Hospital

Miao Ling
National Center for Children's Health: Beijing Children's Hospital

Kaiyi Zhu
National Center for Children's Health: Beijing Children's Hospital

Hailang Sun
National Center for Children's Health: Beijing Children's Hospital

Yuanqi Ji
National Center for Children's Health: Beijing Children's Hospital

XiaoJiao Peng
National Center for Children's Health: Beijing Children's Hospital

Suhui Kuang
National Center for Children's Health: Beijing Children's Hospital

Nan Zhang
National Center for Children's Health: Beijing Children's Hospital

Tianlei Zhang
The second clinical medical college of Wenzhou Medical university

Ming Ge
National Center for Children's Health: Beijing Children's Hospital https://orcid.org/0000-0002-4476-4331

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Abstract

Objective Brain tumors have become the most common solid tumors in children. The epidemiology is poorly described in China. This retrospective study aimed to describe the epidemiologic characteristics, clinical presentation, and prognosis in national health center for children.

Method From January 2015 to December 2020, 484 cases age 0-18 years old diagnosed with brain tumors and receiving neurosurgery treatment were enrolled into the database. Pathology was based on the World Health Organization 2012 nervous system tumor classification, and tumor behavior were classified on International Classification of Diseases for Oncology, third edition. A descriptive and comparative statistic was performed on clinical manifestation, symptom duration, sex, age, tumor location, tumor behavior, and survival time.

Results Among the 484 brain tumors, the median age at diagnosis was 4.62 [2.19, 8.17] years old (4.07 [1.64, 7.13] for benign tumors and 5.36 [2.78, 8.84] for malignant tumors). The overall male to female ratios were 1.33:1, with 1.09:1 and 1.62:1 for benign and malignant tumors respectively. Nausea and vomiting, headache were the most frequent initial symptoms. The median symptoms duration was 4[2, 21] weeks. The three most frequent tumor type were embryonal tumors (22.45%), other astrocytic tumors (20.17%), and diffuse astrocytic tumors (11.02%). Supratentorial tumors comprise 57.38% of all brain tumors. And the most common tumor locations were cerebellum and forth ventricles (38.67%), sellar region (22.87%) and ventricles (10.60%). Male were more common among choroid plexus tumors (63.64%), embryonal tumors (61.11%), ependymal tumors (68.57%), and germ cell tumors (78.13%). Patients were followed for 1 to 82 months. The overall 5-year survival was 77.4%, with 90.0% for benign tumor and 65.3% for malignant tumors. log-rank test found significant different at $p < 0.001$ level.

Conclusion Brain tumors presented particularly sexual, age dependent, and regional dependent epidemiological characteristic. Our results were consistent with previous reports, and might reflect the real epidemiology status in China.

Background

According to the Central Brain Tumor Registry of the United States (CBTRUS) report, brain tumor and other Central nervous system (CNS) tumors have become the most common cancer in the population aged 0-14 years old. Malignant brain tumors have been the most common cause of death in this group. It is known that brain tumors have specific patterns of site distribution and predilection age. Meninges are the most common tumor site was in all ages, with meningioma being the most common tumors histology in the 2021 CBTRUS report[1]. However, pediatric brain tumors have different epidemiologic characteristics compared to the adult population. According to the CBTRUS 2016 report, the most common site of brain tumors was cerebellum, and gliomas was the most common histologic group, of which pilocytic astrocytoma was the majority among 0-14-year-old children[2].

Annual CBTRUS report characterized the pediatric brain tumor in the US, which also hinted racial difference among brain tumors. However, demographic data was seldom reported in Chinese children due to lack of national wide tumor registration system. The only study was Zhou's[3] report which summarized pediatric epidemiologic characteristic with a single center data source from Beijing Tiantan Hospital. However, their data was based on WHO 2000, and uncompleted for lack of prognosis data. Hence, we reviewed all the brain tumors received surgical treatment in Beijing Children's Hospital, National Center for Children's Health from 2015 to 2020, hoping to validate and update the epidemiologic characteristics of pediatric brain tumors in China.

Material And Methods

Data resource

From January 2015 to December 2020, patients between 0-18 years old, diagnosed with brain tumors and received neurosurgery was enrolled into the database. The duplicated data which generated by tumor recurrence or other treatment was deleted. Patients who have been hospitalized but refused neurosurgery or data without pathologic diagnosis were excluded. Demographic information and clinical information including medical history, initial symptoms, pathology, WHO grade, tumor location, surgery date, surgery duration, ventricle peritoneal shunt (V-P shunt), hospital days, medical expenditure was collected. Patients were followed up by telephone or scheduled outpatient recheck. The follow-up items include adjuvant treatment program, survival status, tumor relapse, and death date.

Classification

Histologic diagnosis was based on 2016 WHO Classification of Tumors of the Central Nervous System (2016 WHO classification), and was divided into 17 subgroups. Tumors' behavior was labeled according to the International Classification of Diseases for Oncology, third edition (ICD-O-3), with behavior codes /3 for malignant tumors and /0 or /1 for nonmalignant.

Anatomic location of tumors sites

Tumor location referred to the categories of CBTRUS report and topography code in ICD-O-3. To make it more practical, some details were revised. Fourth ventricle and cerebellum were merged into one group, namely Cerebellum or the fourth ventricle. And the ventricles here referred to lateral ventricles and third ventricle. Sellar region was used to replace the pituitary and craniopharyngeal duct, which included tumors form pituitary and optic chiasma. Cranial nerves refer to all the cranial nerve apart from optic chiasma.

Statistical analysis

Descriptive parameters including mean, median, counts, proportions were calculated with Python 3.7. Mean was used to describe the continues variable, which fit with the normal distribution, and median and

quartile was used to describe the continues variable which did not fit with normal distribution. Kaplan-Meier were used to compute the survival rate. And log-rank test was used to compare the survival curve.

Result

From 2015 to 2020, 484 individuals aged between 0-18 years old diagnosed with brain tumors and received neurosurgery in our center. The median age of this cohort was 4.62 [2.19, 8.17] years old, with male making up 57.02%. The median age at diagnosis of male and female group were 4.79 [2.26, 8.12] and 4.55 [2.14, 8.19] years old respectively. Benign tumors accounted for 53.11% of all brain tumors, of which the median age was 4.07 [1.64, 7.13] years old and male to female ratio was 1.09:1. Distinct to benign brain tumors, malignant brain tumors (46.89%) had a median age of 5.36 [2.78, 8.84] years old and male to female ratio of 1.62:1. Overall, the average hospital days was 19.18 days, and the average medical expenditure was 76147.11 CNY.

Clinical presentations

Overall, the most frequent initial symptom was nausea and vomiting (23.95%), followed by headache (23.43%), motor impairment (12.59%), and epilepsy (10.49%). Other symptoms, such as visual impairment, behavior change, the growth or endocrinal abnormity and so on took up less than 10%. For post fossa tumors cases, the most frequent symptom was headache (32.43%), followed by nausea and vomiting (32.43%), and motor impairment (13.51%). Among sellar tumor individuals, visual impairment (20.93%) was the most common symptom, with headache (15.50%), motor impairment (14.73%), nausea and vomiting (13.95%), and growth or endocrinal abnormity (13.95%) going after. See table 1.

The median duration of symptoms was 4 [2, 21] weeks across all brain tumor cases. Patients with tumors of temporal lobe experience the longest median duration of 18 [4, 51] weeks, followed by other superior tentorial tumors, see table 2. The median duration of symptoms of sellar tumors was 13 [4, 52] weeks, and 4 [3, 13] weeks for cerebellum or forth ventricle tumors. According to the records, about 35.2% (167/475, 9 records did not have a clear description about medical history and was dropped out) of the patients were misdiagnosed in their first visiting of hospital.

Distribution of tumor pathology

Based on the 2016 CNS WHO classification, the most common tumor type is Embryonal tumors (22.45%), followed by Other astrocytic tumors (20.17%), Diffuse astrocytic and oligodendroglial tumors (11.02%) and Craniopharyngioma (10.81%) in sequence. Among benign tumors, the three most common types are other Astrocytic tumors (37.50%), Craniopharyngioma (21.67%), and Neuronal and mixed neuronal-glial tumors (14.58%) in order. Embryonal tumors (44.81%) was the most common type in malignant brain tumors group, with diffuse astrocytic and oligodendroglial tumors (21.99%) and Ependymal tumors (14.52%) coming after. Among Embryonal tumors, the most common pathology was medulloblastoma, making up 82.41%. See Figure 1.

Distribution of tumor sites

Supratentorial tumors comprise 57.38% of all brain tumors. Overall, most of the brain tumors situated in Cerebellum or the fourth ventricle (38.67%), and sellar region (22.87%). Benign and malignant tumors had significantly different patterns of site distribution. In the benign tumors group, the most common site was the sellar region (40.00%), with Cerebellum or the fourth ventricle (24.58%) and Ventricles (17.08%) following behind. In regards to malignant brain tumors group, Cerebellum or the fourth ventricle (52.70%) is the most common site, with other sites share an even proportion. See Figures 2 ~ 3.

In the cerebellum or fourth ventricle, embryonal tumors (50.54%) was the most common tumor type, making up more half of the total. The second and third most common tumor type in this place were other astrocytic tumors (24.73%) and ependymal tumors (9.14%). See Figure 4.

In the sellar region, the most three common pathologies were Craniopharyngioma (47.27%), other astrocytic tumors (35.45%) and germ cell tumors (5.45%) in sequence. See Figure 4.

Sex and age distribution

Across all brain tumors, the proportion of male (57.17%) was a little greater than female (42.83%). Sex distribution varied a lot with different tumor pathologies. Male (52.08%) and female (47.92%) shared the similar proportion in benign tumors, while males (62.24%) were more common than females (37.76%) in malignant tumors. Specifically, there were no obvious sex bias in Astrocytic tumors, Diffuse astrocytic and oligodendroglial tumors, Neuronal and mixed neuronal-glial tumors and craniopharyngioma. However, male made up higher proportion than female among Embryonal tumors, Ependymal tumors, Pineal tumors, Germ cell tumors, and Choroid plexus tumors. See Figures 5 ~ 6.

The median age varies a lot with different histologic types of brain tumors. See Figure 7. Ependymal tumors (4.10[2.14, 7.60]), Embryonal tumors (5.93[2.96,8.87]), Germ cell tumors (9.30[4.15, 10.99]), Craniopharyngioma (7.74[3.53,8.21]), Meningiomas (11.98[7.85, 13.19]), and metastatic tumors (5.54[4.96, 6.88]) all had the median age older than 3 years old, while Pineal tumors (1.52[1.49, 1.77]), Choroid plexus tumors (0.73[0.44, 1.51]) generally influenced the children younger than 3 years old. In embryonal tumors, age difference was still noted. The median age of medulloblastoma was 6.93[4.12, 9.75] years old, while it was 2.30[1.34, 2.74] years old for AT/RT patients.

Survival

Patients were followed up for 1 to 82 months. There were 54 patients missed during the following up. The overall 5-year survival rate was 77.4% in the 430 brain tumors, with a median survival time of 81.0 months. Malignant and benign tumors had the 5-year survival rate of 65.3% and 90.0% respectively. The median survival time of malignant tumors was 76.0 months. Given that more than half of the benign brain tumor patients remained alive, it was unfeasible to calculate the median survival time of benign tumors. Log-rank test found a significant difference between the two groups($p<0.001$). See Figure 8.

Discussion

Central nervous system (CNS) tumors account for a quater of all childhood cancers, and has been the most common solid tumors, of which brain tumors takes up the majority[4-6]. In the United States, brain tumors make up more than 1% of newly diagnosed cancer cases[7]. Despite of improved treatment for the past years, brain tumors are still the leading cause of cancer-related death among children[8]. Brain tumors are heterogeneous, which varies from race, gender, age and so on[9-11]. The epidemic studies in China are scare and are based on dated CNS WHO classification[3]. Hence it is meaningful to summary and validate the epidemic information again. Besides, this study collected and described other important information, such as medical expenditure, manifestation, prognosis and so on.

Presentations

The most frequent initial symptoms were nausea and vomiting (23.95%), and headache (23.43%). Motor impairment only accounted for 12.59% of all brain tumor children. The results are consistent with a previous meta study[12]. Manifestations are associated with brain tumors' location. Visual impairment is frequently seen in sellar tumor, while nausea and vomiting, and headache are more common in cerebellum and forth ventricle tumors. Due to these common symptoms are not specific to CNS tumors, it might lead to misdiagnosis and delay of diagnosis. Our data showed the rate of misdiagnosis reached to 32.5%. We found that superior tentorial tumors are more insidious than inferior tentorial tumors. The general median duration of symptoms across all brain tumors is 4 weeks, while tumors of temporal lobe experience the longest duration for median of 18 weeks. General median symptom duration of posterior fossa tumors is 4 weeks. This result implies that the diagnostic capability in China has reached to the international level[13]. However, the longest symptom duration of posterior fossa tumors was more than 10 years. Increasing awareness of the varied and complex symptomatology that often occurs with CNS tumors in China is necessary and could help reduce misdiagnosis and achieve early diagnosis.

Predilection age

The number of brain tumors cases decrease with advancing age, which is consistent with the CBTRUS 2015 report (apart from tumors of pituitary)[2]. The median age of the group was 4.62 [2.19, 8.17] years old years old, with median age of malignant tumor 5.36 [2.78, 8.84] years old, a bit of older than the benign group of 4.07 [1.64, 7.13] years old. This trend is consistent of a previous report[11]. However the recent CBTRUS indicates that malignant tumors tend to affect younger children compared with non-malignant tumors[1]. This might be due to the sampling bias on tumor histology. Benign tumors of pituitary tend to affect adolescents (15-19 years old), which will cause an increase in median age of benign tumors group, which were not sufficiently enrolled in our data. Our data shows that craniopharyngioma, ependymal tumors, embryonal tumors, metastatic tumors, germ cell tumors, meningiomas and tumors of Cranial and paraspinal nerves tend to affect older children, while choroid plexus tumors, melanocytic tumors, tumors of pineal region, neuronal and mixed neuronal-glial tumor, and astrocytomas prefer to affect infants and toddlers. This is in according with previous CBTRUS reports[14].

Sex

Across all brain tumors, sex distribution is almost balanced, with a male to female ratio of 1.33:1. However, In the subgroup analysis, males took up a greater proportion in malignant tumors than benign tumors (62.9% vs 52.1%). This is in accordance with the previous report that malignant tumors occurring much more frequently in males[9]. We found that sex difference varies by histology. Germ cell tumors, embryonal tumors, ependymal tumors, and choroid plexus tumors see more males than females, while little gender bias is noted in gliomas (including diffuse astrocytic and oligodendroglial tumors, other astrocytic tumors, and neuronal and mixed neuronal-glial tumors) and craniopharyngioma. These results is similar with the data of CBTRUS report[1].

Location

Same as the previous studies, supratentorial tumors are preponderant (57.38%) compared with infratentorial tumors (42.62%). To be specific, the most three common sites are the cerebellum or fourth ventricle, sellar region and ventricles. This is a little different from the CBTRUS report[1], which showed that the three most common sites are sellar region, the cerebellum and other brain. Furthermore, proportion of tumors in cerebellum in our center is about two times of that in the US. This might be due to that we put tumors in cerebellar and forth ventricle into one group, but CBTRUS did not classify tumor in this way. Given the difficulty to differentiate tumors of cerebellum or the fourth ventricle in magnetic resonance image (MRI), we believe it is more applicable to categorize these two sites into one group site. Besides, our data is lack of population aged between 15-19 years old who are fragile to sellar region tumors. When looking the benign and malignant groups respectively, the sites distribution pattern is different. The most common site in malignant tumors is the cerebellum or fourth ventricles, while sellar region is the most common site in benign tumors. In the cerebellum or forth ventricle, embryonal tumors (account for almost 50% of tumors in this area), other astrocytic tumors and ependymal tumors are the top three types. And in sellar region, the most three common types are craniopharyngioma, astrocytoma and germ cell tumors. In the ventricles, choroid plexus tumors, germ cell tumors, and other astrocytic tumors are the three most common types. This is in accordance with previous studies[15]. With these figures, our data might help Chinese clinicians have better understanding of differential diagnosis of pediatric brain tumors.

Pathology

This study is based on WHO 2016 classification, which is different form the existing studies. Tumors accounting for less than 5% were assigned into “others group”. Above all, the most common pathology type was embryonal tumors accounting for 22.45% of all brain tumors, followed by other astrocytic tumors and diffuse astrocytic and oligodendroglial tumors. This is consistent with a previous study about Chinese population[3]. However, CBTRUS reported that pilocytic astrocytoma is the most common pathology type[1, 2, 9, 14]. This is due to different approaches of classification. We put all the embryonal tumors into one group, leading to the increase in the proportion of embryonal tumors. Distinguished with a previous study in China[3], we showed that medulloblastoma was more frequent than

craniopharyngioma, and ependymal tumors was more common than GCTs, which is consistent with the previous reports[14, 16, 17]. We speculate, there might exist the sample bias in the previous chinses report. Because, it is not a children hospital, and the younger patient might prefer to refer to a children hospital, rather than a general hospital. GCTs only takes up 6.65% of the whole brain tumors, which is similar with the investigation in China, but distinguished from other reported in Japan, Taiwan (China) and far eastern countries with an incidence of 10–14% of the brain tumors. This difference might be explained that patients with germinomas often undergo nonsurgical treatments, the actual number of GCTs might be significantly underestimated in this study.

Survival

It is known that survival of patients with brain tumors varies by histology, age at diagnosis, tumor location and so on. And Our data showed that the 5-year overall survival (OS) of benign tumors was 90.0%, consistent with previous studies. In the United States, 96% of children 0–19 years old with nonmalignant tumors survived 10 years after diagnosis[18]. Tore Stokland[19] reported that the 5-years overall survival (OS) of low grade glioma (LGG) up to 96.4%. However, the outcome of LGG could be variable with extent of resection. If complete surgical resection is possible, 10-year progression-free survival (PFS) exceeds 85%, but drops below 50% if there is radiologically visible residual tumor[20]. Sahaja Acharya[21] reported the 10-years OS of LGG reached to 76.4% (high risk) ~ 95.6% (low risk). Alvaro Lassaletta[22] reported the 10-year progression-free survival are 27% and 60.2% respectively in BRAF VE600 mutation and wild type cohort. Overall survival of craniopharyngioma (CP)ranges from 83% to 96% at 5 years[23], from 65% to 100% at 10 years[24-26] and is, on average, 62% at 20 years. At present whether age at diagnosis of CP, sex, and pathologic subtype are prognostic factors for survival remain controversial[27].

The 5-year OS of malignant tumors was 65.3%, similar with previous reports(75.4%)[1]. The 10-year survival for children ages 0–19 diagnosed with malignant brain and other CNS tumors was estimated at 72% with lowest (17%) being attributable to glioblastoma[11]. Other studies reported that less than 5.5% Glioblastoma survived more than 5 years[28, 29]. Another malignant tumor, diffuse intrinsic pontine glioma (DIPG) had an overall survival of less than 1 year generally[30]. Atypical teratoid/rhabdoid tumor (AT/RT) was reported to had a four years OS of 43%[31], and another study reported a 6-year OS of 35% [32]. High dose chemotherapy and radiation therapy were associated with better survival, while tumour metastasis, intrathecal chemotherapy and extent of resection do not significantly affect survival[33]. All in all, the prospect of malignant tumors remains unsatisfied and more resource need to be introduced in this fields. Due to the limitation of sample size, we did not calculate the survial rate of the specific tumor type. We hope to add this analysis in the future study.

So far, little information of epidemiology about Chinese is known. As national center for children's health, we summarized out data and hope that our experience could provide more information about pediatric brain tumors in China. At the same time, we acknowledge that due to lack of national wide registration system of brain tumors, there might exist some inevitable bias. Apart from that, children aged from 15-18

in China prefer to general hospitals, rather than children's hospital. Hence, the number patients of adolescence are relatively small in this study.

Al in all, epidemiology of brain tumors in our center presented similar pattern with previous reports. Ratio of benign and malignant tumors approach to 1:1.03. And males are more vulnerable to malignant tumors. The site distribution patterns of benign and malignant brain tumors are significantly different. These demographic characteristics provide us further understanding of pediatric brain tumors, like sex predisposition, predilection age of onset. And our data might be able to reflect the real situation of pediatric brain tumors in Chinese.

Declarations

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Author Contributions

Ming Ge, Wei Yang, and Yingjie Cai contributed to the study conception and design. Material preparation, data collection were performed by Jiashu Chen, Ping Yang, Zesheng Ying, Yuting Liang, Miao Ling, Hailang Sun, Yuanqi Ji, XiaoJiao Peng, Suhui Kuang, Tianlei Zhang, and data analysis were performed by Wei Yang and Kaiyi Zhu. Pathology reconfirmation was performed by Nan Zhang3. The first draft of the manuscript was written by Wei Yang and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data Availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval

This is an observational study. The Ethic Community of Beijing Children's Hospital has confirmed that no ethical approval is required.

Informed consent

This is a retrospective study, and there are no identifying details in our manuscript. No written consent was acquired from participates.

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References

1. Ostrom QT, Patil N, Cioffi G, Waite K, Kruchko C, Barnholtz-Sloan JS (2020) CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2013–2017. Neuro-Oncology 22: iv1-iv96 doi:10.1093/neuonc/noaa200 %J Neuro-Oncology
2. Ostrom QT, de Blank PM, Kruchko C, Petersen CM, Liao P, Finlay JL, Stearns DS, Wolff JE, Wolinsky Y, Letterio JJ, Barnholtz-Sloan JS (2014) Alex's Lemonade Stand Foundation Infant and Childhood Primary Brain and Central Nervous System Tumors Diagnosed in the United States in 2007–2011. Neuro-Oncology 16: x1-x36 doi:10.1093/neuonc/nou327 %J Neuro-Oncology
3. Zhou D, Zhang Y, Liu H, Luo S, Luo L, Dai K (2008) Epidemiology of nervous system tumors in children: a survey of 1,485 cases in Beijing Tiantan Hospital from 2001 to 2005. Pediatr Neurosurg 44: 97-103 doi:10.1159/000113110
4. Cacciotti C, Fleming A, Ramaswamy V (2020) Advances in the molecular classification of pediatric brain tumors: a guide to the galaxy. J Pathol 251: 249-261 doi:10.1002/path.5457
5. Udaka YT, Packer RJ (2018) Pediatric Brain Tumors. Neurol Clin 36: 533-556 doi:10.1016/j.ncl.2018.04.009
6. Hsu W, Jallo GI (2013) Chapter 100 - Pediatric spinal tumors. In: Dulac O, Lassonde M, Sarnat HB (eds) Handbook of Clinical Neurology. Elsevier, pp 959-965
7. Ostrom QT, Adel Fahmideh M, Cote DJ, Muskens IS, Schraw JM, Scheurer ME, Bondy ML (2019) Risk factors for childhood and adult primary brain tumors. Neuro Oncol 21: 1357-1375 doi:10.1093/neuonc/noz123
8. Bornhorst M, Hwang EI (2020) Molecularly Targeted Agents in the Therapy of Pediatric Brain Tumors. Paediatr Drugs 22: 45-54 doi:10.1007/s40272-019-00369-z
9. Ostrom QT, Gittleman H, Truitt G, Boscia A, Kruchko C, Barnholtz-Sloan JS (2018) CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2011-2015. Neuro Oncol 20: iv1-iv86 doi:10.1093/neuonc/noy131
10. Barnholtz-Sloan JS, Severson RK, Stanton B, Hamre M, Sloan AE (2005) Pediatric brain tumors in non-Hispanics, Hispanics, African Americans and Asians: differences in survival after diagnosis. Cancer Causes Control 16: 587-592 doi:10.1007/s10552-004-7843-2
11. Adel Fahmideh M, Scheurer ME (2021) Pediatric Brain Tumors: Descriptive Epidemiology, Risk Factors, and Future Directions. Cancer Epidemiol Biomarkers Prev 30: 813-821 doi:10.1158/1055-9965.EPI-20-1443
12. Wilne S, Collier J, Kennedy C, Koller K, Grundy R, Walker D (2007) Presentation of childhood CNS tumours: a systematic review and meta-analysis. Lancet Oncol 8: 685-695 doi:10.1016/S1470-2045(07)70207-3

13. HeadSmart Be Brain Tumour A (2016) A new clinical guideline from the Royal College of Paediatrics and Child Health with a national awareness campaign accelerates brain tumor diagnosis in UK children–"HeadSmart: Be Brain Tumour Aware". Neuro Oncol 18: 445-454 doi:10.1093/neuonc/nov187
14. Ostrom QT, Cioffi G, Waite K, Kruchko C, Barnholtz-Sloan JS (2021) CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2014-2018. Neuro Oncol 23: iii1-iii105 doi:10.1093/neuonc/noab200
15. Bettegowda C, Adogwa O, Mehta V, Chaichana KL, Weingart J, Carson BS, Jallo GI, Ahn ES (2012) Treatment of choroid plexus tumors: a 20-year single institutional experience. J Neurosurg Pediatr 10: 398-405 doi:10.3171/2012.8.PEDS12132
16. Wong TT, Ho DM, Chang KP, Yen SH, Guo WY, Chang FC, Liang ML, Pan HC, Chung WY (2005) Primary pediatric brain tumors: statistics of Taipei VGH, Taiwan (1975-2004). Cancer 104: 2156-2167 doi:10.1002/cncr.21430
17. Kadri H, Mawla AA, Murad L (2005) Incidence of childhood brain tumors in Syria (1993-2002). Pediatr Neurosurg 41: 173-177 doi:10.1159/000086557
18. Ostrom QT, Cioffi G, Gittleman H, Patil N, Waite K, Kruchko C, Barnholtz-Sloan JS (2019) CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2012-2016. Neuro Oncol 21: v1-v100 doi:10.1093/neuonc/noz150
19. Stokland T, Liu JF, Ironside JW, Ellison DW, Taylor R, Robinson KJ, Picton SV, Walker DA (2010) A multivariate analysis of factors determining tumor progression in childhood low-grade glioma: a population-based cohort study (CCLG CNS9702). Neuro Oncol 12: 1257-1268 doi:10.1093/neuonc/noq092
20. Wisoff JH, Sanford RA, Heier LA, Sposto R, Burger PC, Yates AJ, Holmes EJ, Kun LE (2011) Primary neurosurgery for pediatric low-grade gliomas: a prospective multi-institutional study from the Children's Oncology Group. Neurosurgery 68: 1548-1554; discussion 1554-1545 doi:10.1227/NEU.0b013e318214a66e
21. Acharya S, Liu JF, Tatevossian RG, Chiang J, Qaddoumi I, Gajjar A, Walker D, Harreld JH, Merchant TE, Ellison DW (2020) Risk stratification in pediatric low-grade glioma and glioneuronal tumor treated with radiation therapy: an integrated clinicopathologic and molecular analysis. Neuro Oncol 22: 1203-1213 doi:10.1093/neuonc/noaa031
22. Lassaletta A, Zapotocky M, Mistry M, Ramaswamy V, Honnorat M, Krishnatry R, Guerreiro Stucklin A, Zhukova N, Arnoldo A, Ryall S, Ling C, McKeown T, Loukides J, Cruz O, de Torres C, Ho CY, Packer RJ, Tatevossian R, Qaddoumi I, Harreld JH, Dalton JD, Mulcahy-Levy J, Foreman N, Karajannis MA, Wang S, Snuderl M, Nageswara Rao A, Giannini C, Kieran M, Ligon KL, Garre ML, Nozza P, Mascelli S, Raso A, Mueller S, Nicolaides T, Silva K, Perbet R, Vasiljevic A, Faure Conter C, Frappaz D, Leary S, Crane C, Chan A, Ng HK, Shi ZF, Mao Y, Finch E, Eisenstat D, Wilson B, Carret AS, Hauser P, Sumerauer D, Krskova L, Larouche V, Fleming A, Zelcer S, Jabado N, Rutka JT, Dirks P, Taylor MD, Chen S, Bartels U, Huang A, Ellison DW, Bouffet E, Hawkins C, Tabori U (2017) Therapeutic and Prognostic Implications

of BRAF V600E in Pediatric Low-Grade Gliomas. J Clin Oncol 35: 2934-2941 doi:10.1200/JCO.2016.71.8726

23. Müller HL, Bueb K, Bartels U, Roth C, Harz K, Graf N, Korinthenberg R, Bettendorf M, Kühl J, Gutjahr P, Sörensen N, Calaminus G (2001) Obesity after childhood craniopharyngioma–German multicenter study on pre-operative risk factors and quality of life. Klinische Padiatrie 213: 244-249 doi:10.1055/s-2001-16855
24. Poretti A, Grotzer MA, Ribi K, Schonle E, Boltshauser E (2004) Outcome of craniopharyngioma in children: long-term complications and quality of life. Dev Med Child Neurol 46: 220-229 doi:10.1017/s0012162204000374
25. Visser J, Hukin J, Sargent M, Steinbok P, Goddard K, Fryer C (2010) Late mortality in pediatric patients with craniopharyngioma. J Neurooncol 100: 105-111 doi:10.1007/s11060-010-0145-5
26. Karavitaki N, Brufani C, Warner JT, Adams CB, Richards P, Ansorge O, Shine B, Turner HE, Wass JA (2005) Craniopharyngiomas in children and adults: systematic analysis of 121 cases with long-term follow-up. Clin Endocrinol (Oxf) 62: 397-409 doi:10.1111/j.1365-2265.2005.02231.x
27. Muller HL, Merchant TE, Warmuth-Metz M, Martinez-Barbera JP, Puget S (2019) Craniopharyngioma. Nat Rev Dis Primers 5: 75 doi:10.1038/s41572-019-0125-9
28. Ostrom QT, Gittleman H, Liao P, Vecchione-Koval T, Wolinsky Y, Kruchko C, Barnholtz-Sloan JS (2017) CBTRUS Statistical Report: Primary brain and other central nervous system tumors diagnosed in the United States in 2010-2014. Neuro Oncol 19: v1-v88 doi:10.1093/neuonc/nox158
29. Jansen M, Yip S, Louis DN (2010) Molecular pathology in adult gliomas: diagnostic, prognostic, and predictive markers. Lancet Neurol 9: 717-726 doi:10.1016/S1474-4422(10)70105-8
30. Lapin DH, Tsoli M, Ziegler DS (2017) Genomic Insights into Diffuse Intrinsic Pontine Glioma. Front Oncol 7: 57 doi:10.3389/fonc.2017.00057
31. Reddy AT, Strother DR, Judkins AR, Burger PC, Pollack IF, Krailo MD, Buxton AB, Williams-Hughes C, Fouladi M, Mahajan A, Merchant TE, Ho B, Mazewski CM, Lewis VA, Gajjar A, Vezina LG, Booth TN, Parsons KW, Poss VL, Zhou T, Biegel JA, Huang A (2020) Efficacy of High-Dose Chemotherapy and Three-Dimensional Conformal Radiation for Atypical Teratoid/Rhabdoid Tumor: A Report From the Children's Oncology Group Trial ACNS0333. J Clin Oncol 38: 1175-1185 doi:10.1200/JCO.19.01776
32. Bartelheim K, Nemes K, Seeringer A, Kerl K, Buechner J, Boos J, Graf N, Durken M, Gerss J, Hasselblatt M, Kortmann RD, Teichert von Luettichau I, Nagel I, Nygaard R, Oyen F, Quiroga E, Schlegel PG, Schmid I, Schneppenheim R, Siebert R, Solano-Paez P, Timmermann B, Warmuth-Metz M, Fruhwald MC (2016) Improved 6-year overall survival in AT/RT - results of the registry study Rhabdoid 2007. Cancer Med 5: 1765-1775 doi:10.1002/cam4.741
33. Schrey D, Carceller Lechon F, Malietzis G, Moreno L, Dufour C, Chi S, Lafay-Cousin L, von Hoff K, Athanasiou T, Marshall LV, Zacharoulis S (2016) Multimodal therapy in children and adolescents with newly diagnosed atypical teratoid rhabdoid tumor: individual pooled data analysis and review of the literature. J Neurooncol 126: 81-90 doi:10.1007/s11060-015-1904-0

Tables

Table 1 Summaries of Initial symptoms

Initial symptoms	Overall (n, %)		Cerebellum or fourth ventricles (n, %)		Sellar region (n, %)		Ventricles (n, %)	
Nausea and vomiting	137	23.95%	72	32.43%	18	13.95%	14	25.93%
Headache	134	23.43%	81	36.49%	20	15.50%	6	11.11%
Motor impairment	72	12.59%	30	13.51%	19	14.73%	6	11.11%
Epilepsy	60	10.49%	6	2.70%	6	4.65%	3	5.56%
Visual impairment	54	9.44%	12	5.41%	27	20.93%	6	11.11%
By accident	33	5.77%	7	3.15%	7	5.43%	7	12.96%
Abnormal behaviors	29	5.07%	5	2.25%	8	6.20%	5	9.26%
Growth and endocrine dyscrasia	25	4.37%	2	0.90%	18	13.95%	2	3.70%
Cranial nerve impairment	9	1.57%	2	0.90%	2	1.55%	-	-
Abnormal head appearance	9	1.57%	1	0.45%	1	0.78%	4	7.41%
Head tilt	6	1.05%	4	1.80%	-	-	-	-
Abnormal temperature	3	0.52%	-	-	3	2.33%		
Pat the head	1	0.17%	-	-	-	-	1	1.85%

Table 2 Duration of symptoms

	Duration of symptoms (weeks)					
Tumor Location	**count**	**min**	**25%**	**50%**	**75%**	**max**
Temporal lobe of brain	35	0	4	18	51	365
Other brain regions	9	3	4	14	35	365
Occipital lobe of brain	1	13	13	13	13	13
Sellar region	104	0	4	13	52	309
Parietal lobe of brain	19	0	1.5	9	11.5	77
Pineal region	16	0	2	5	10	51
Brain stem	19	0	1.5	4	5	77
Cerebellum or the fourth ventricle	186	0	3	4	13	617
Frontal lobe of brain	33	0	3	4	10	104
Ventricles	51	0	2	3	9	261
Meninges	2	0	1	2	3	4

Table 3 Tumor site grouping

Sites	Note
Frontal lobe of brain	
Temporal lobe of brain	
Parietal lobe of brain	
Occipital lobe of brain	
Sellar region	Including Optic glioma in optic chiasma
Pineal region	
Cerebrum	
Ventricle	The fourth ventricle is not included
Cerebellum or the fourth ventricle	
Brain stem	
Other brain regions	
Cranial nerves	
Meninges	

Figures

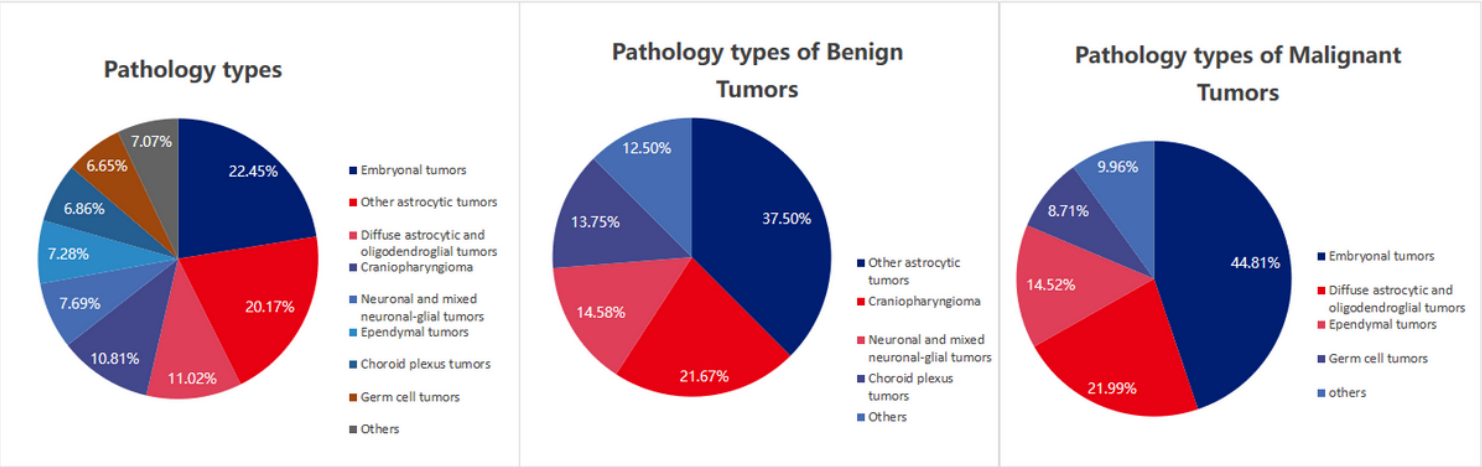

Figure 1

Distribution of tumor types in Children (Age 0-18 Years) of Primary Brain Tumors from 2015-2020

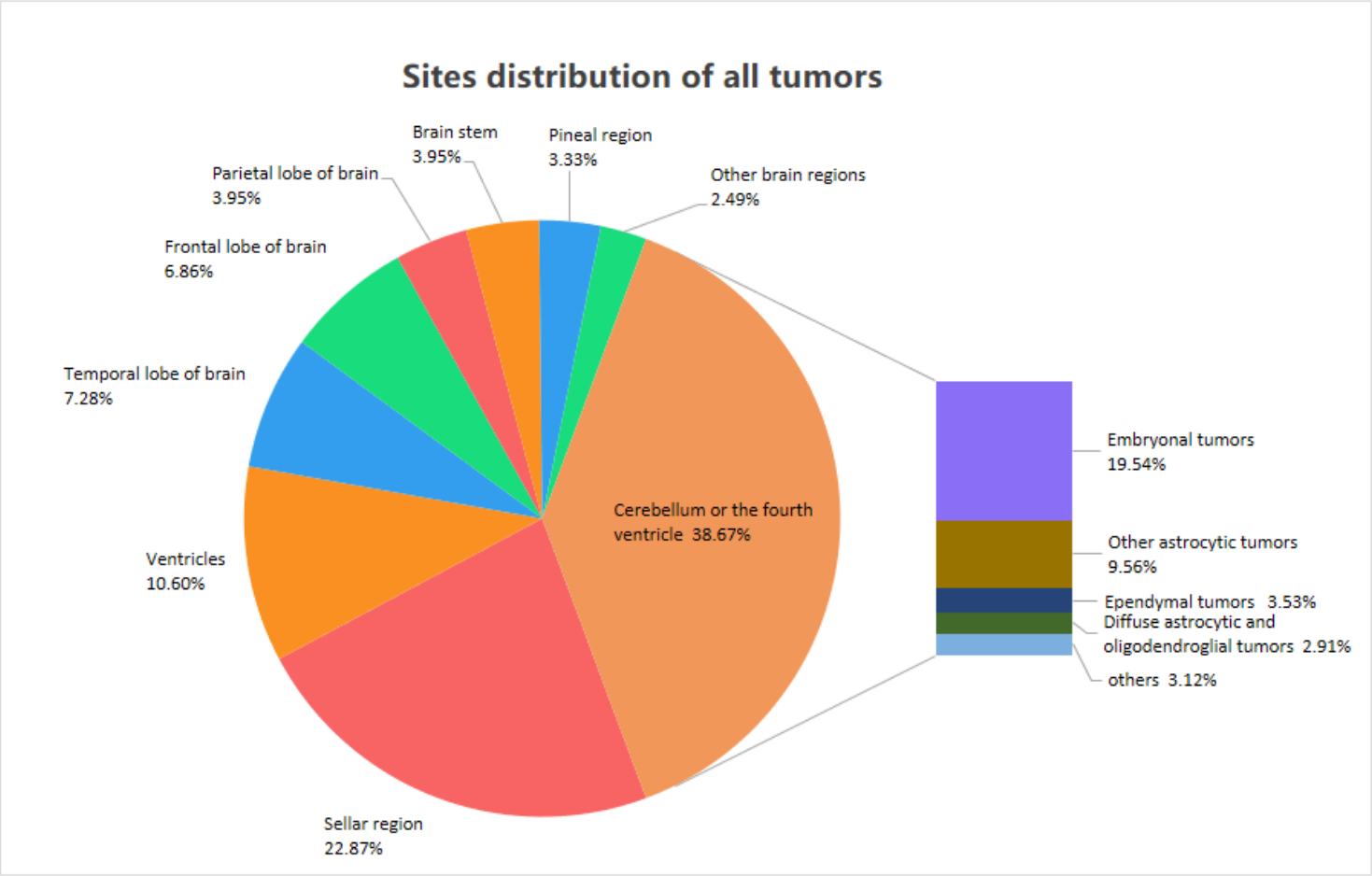

Figure 2

Distribution of tumor sites in Children (Age 0-18 Years) of Primary Brain Tumors from 2015-2020

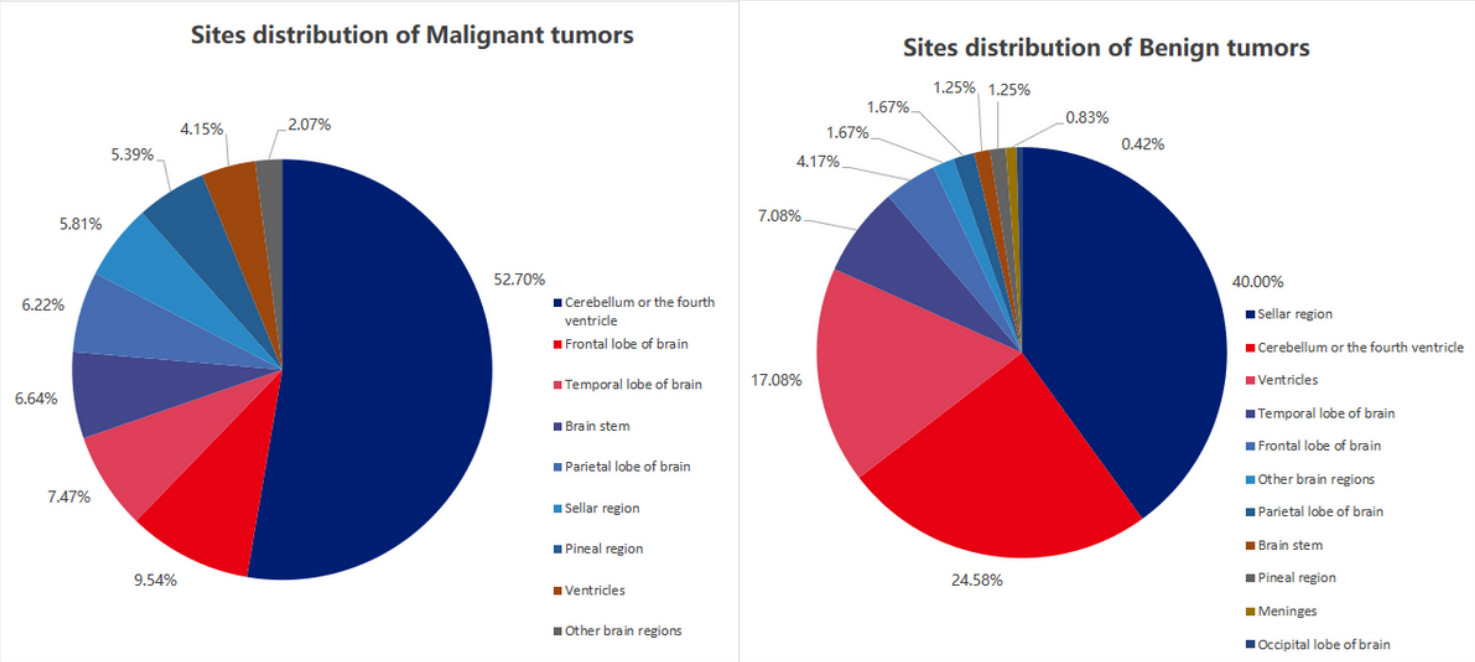

Figure 3

Distribution of malignant and benign tumor sites in Children (Age 0-18 Years) of Primary Brain Tumors from 2015-2020

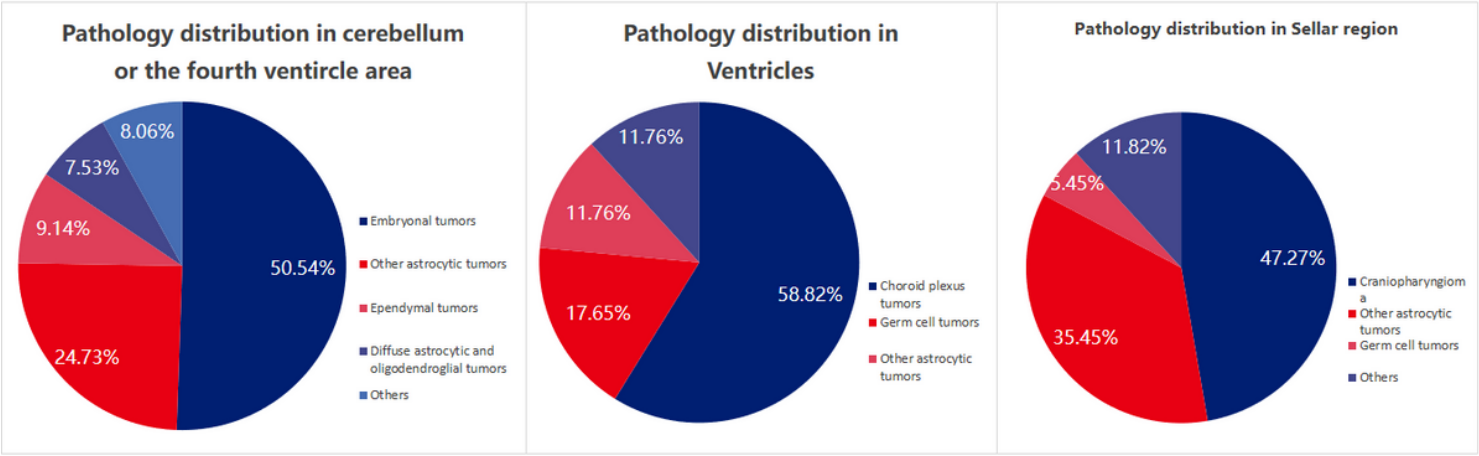

Figure 4

Pathology poportions of the most three common tumor sites in Children (Age 0-18 Years) of Primary Brain Tumors from 2015-2020

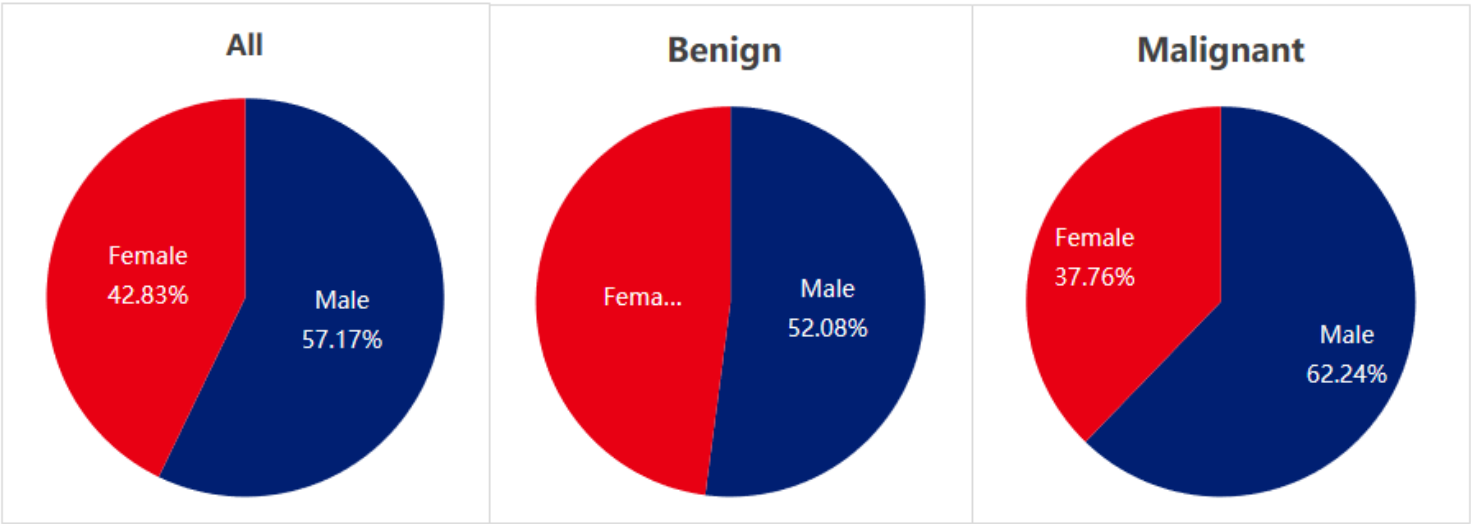

Figure 5

Sex distribution in Children (Age 0-18 Years) of Primary Brain Tumors from 2015-2020

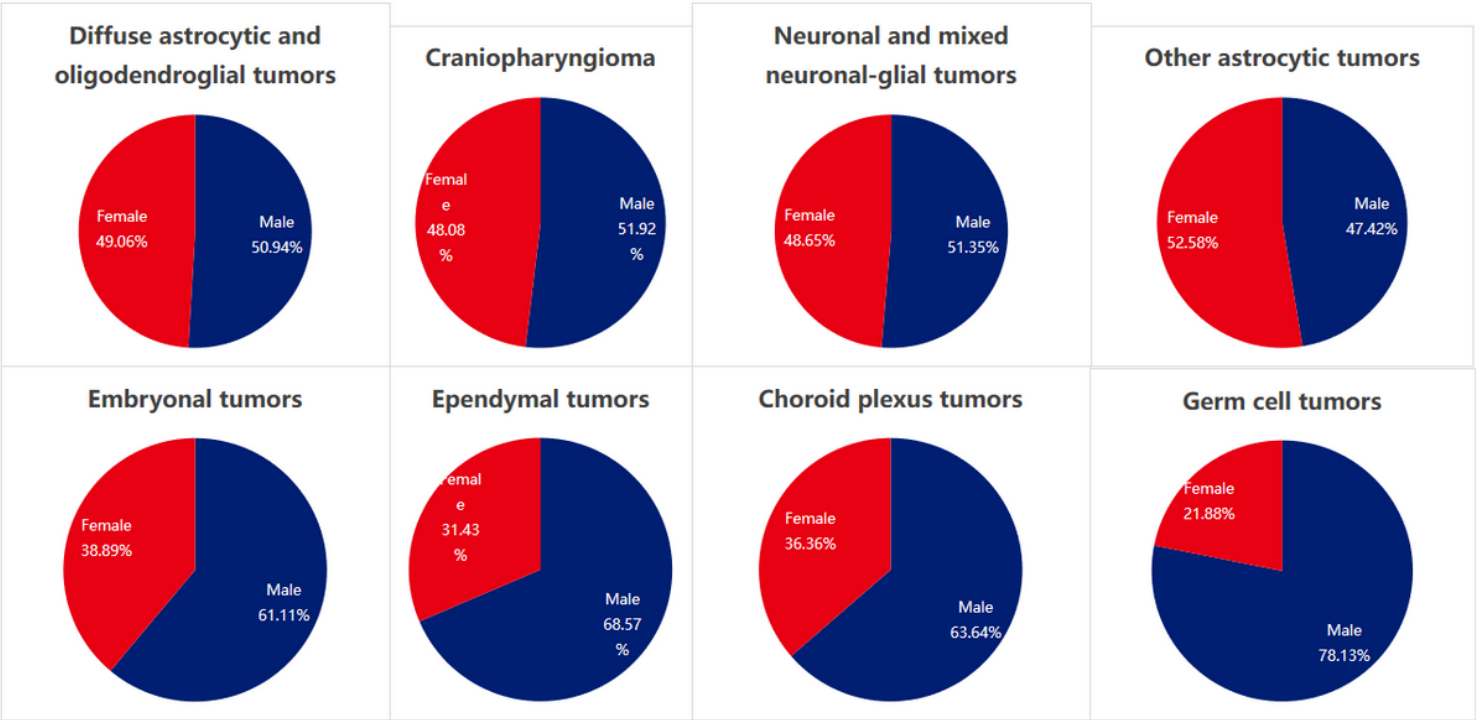

Figure 6

Sex distribution of specific tumor types in Children (Age 0-18 Years) of Primary Brain Tumors from 2015-2020

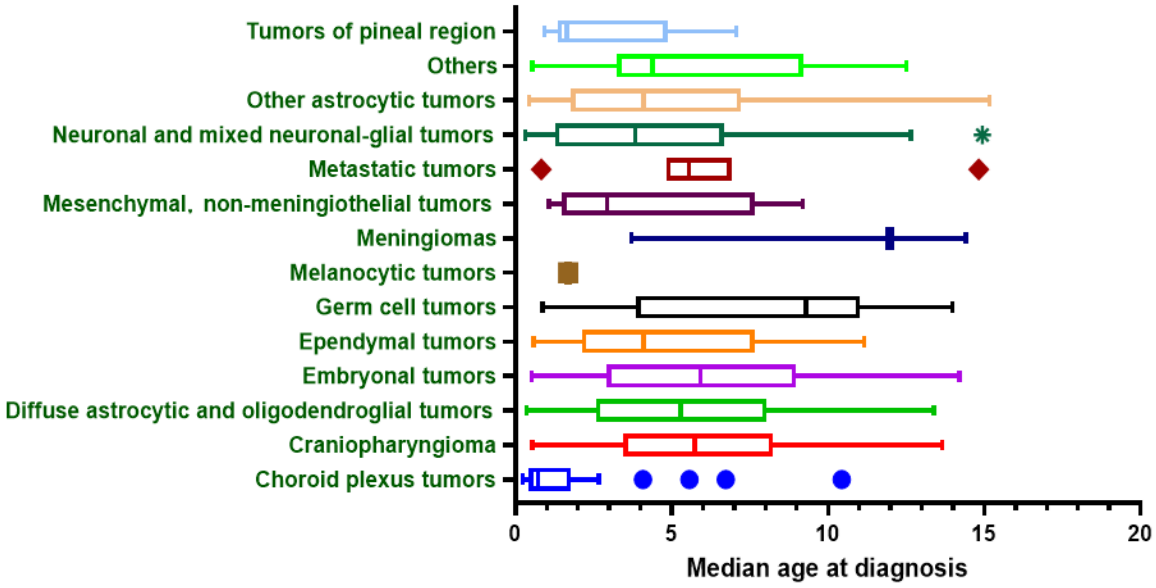

Figure 7

Median age of different tumor types in Children (Age 0-18 Years) of Primary Brain Tumors from 2015-2020

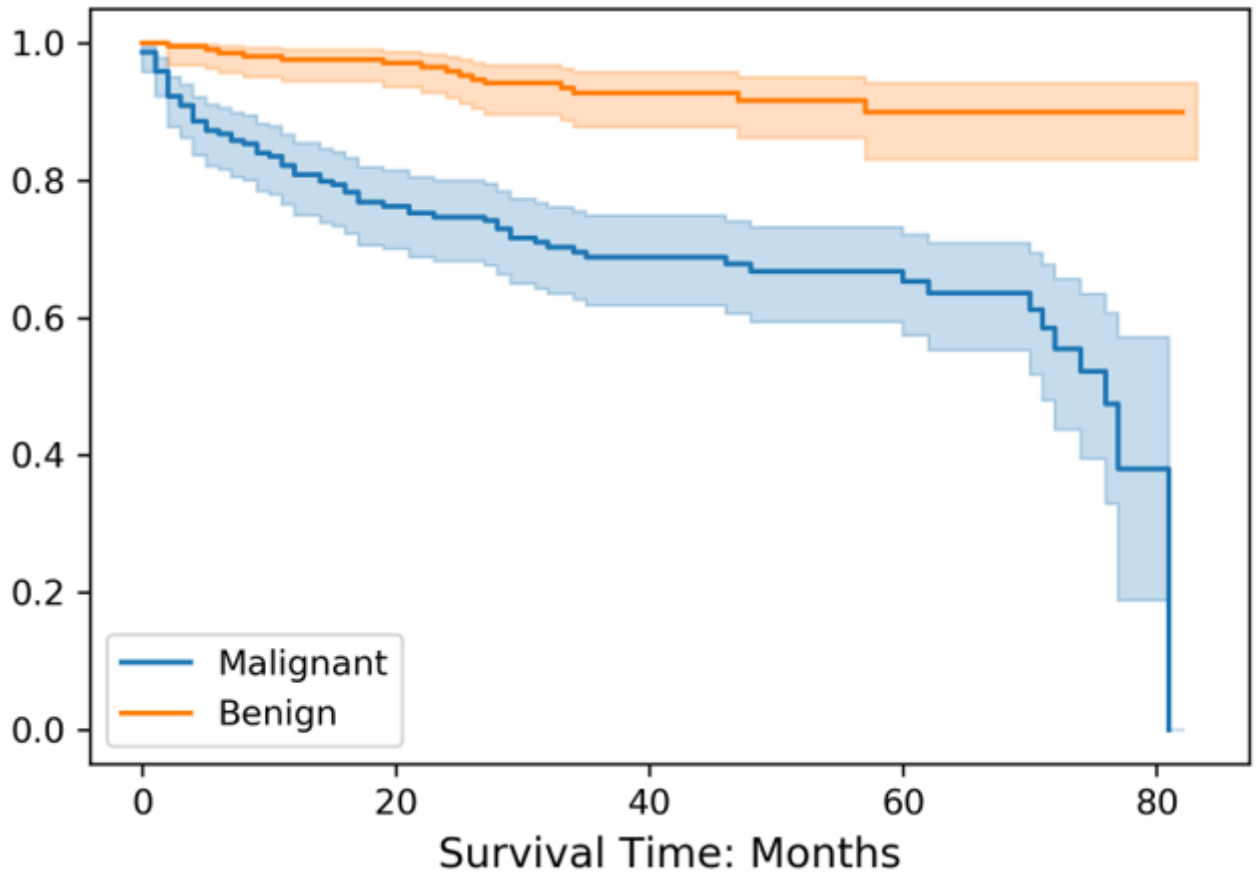

Figure 8

Survival curve of malignant and benign tumors in Children (Age 0-18 Years) of Primary Brain Tumors from 2015-2020