Original Article

Brain Tumor in Childhood: A Study of 132 cases based on the World Health Organization Classification 2000

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Abstract Brain tumors are one of the common neoplasms in children worldwide. Using the recent World Health Organization classification of the nervous system neoplasms, we reported a series of 132 brain tumors that occurred in children 15 years of age or younger (mean 7.89 years) was reported. All cases were diagnosed during August 2001 - December 2004 at the Institute of Pathology, Department of Medical Services, and Department of Pathology, Faculty of Medicine, Chulalongkorn University, Bangkok. Boys were twice more commonly affected than girls, with the supratentorium to infratentorium ratio of 1.6: 1. Neuroepithelial tumors such as astrocytomas (25.0%), ependymomas (18.9%), and embryonal tumors (14.4%) constituted the majority of the series. An incidence of germ cell tumors (12.9%) was comparable to those of other Asian populations, but was higher than those recognized in the Western countries. The common posterior fossa tumors included ependymal neoplasms (14.4%), medulloblastoma (11.4%), and pilocytic astrocytoma (6.1%). Although relatively uncommon, several tumor entities previously undocumented in Thai series of brain tumors have emerged in the current study. These included 5 subependymal giant cell astrocytomas, 3 dysembryoplastic neuroepithelial tumors, 2 atypical teratoid/rhabdoid tumors, 1 pleomorphic xanthoastrocytoma, 1 desmoplastic infantile ganglioglioma, and 1 low grade hypothalamic neuronal tumor. Recognition of these recently-described tumor entities is important for correct diagnosis and proper management of the patients.

Key words: **brain tumors, childhood, WHO classification**

Introduction

Brain tumors are the second most common neoplasm in children worldwide, preceded only by leukemia.[1,2] Based on the largest series of 2,897 neural neoplasms in Thailand from Chulalongkorn and Siriraj hospitals, 292/1,028 intracranial tumors (28.4%) affected children under 15 years of age.[3] Another study from

Ramathibodi Hostpital, which specifically paid attention to pediatric brain tumors (427 cases), disclosed a male to female ratio of 1.3 to 1 and the supratentorium to infratentorium ratio of 1 to 1.03.[4] Astrocytic neoplasms are the most common tumors (41%), followed by medulloblastoma (22%).[4]

Attempts have been made for many years to classify brain tumors, and the most widely used classification now is that of the World Health Organization (WHO). First published in 1979, the WHO classification of brain tumors has been revised twice in 1993 and then in 2000.[5-7]As a result of clinicopathological studies, advances in modern techniques, and international collaborations; several new entities, namely dysembryoplastic neuroepithelial tumor and central neurocytoma, have been recognized while some (such as polar spongioblastoma) became obsolete. To our best knowledge, no series of pediatric brain tumors in Thailand have been analyzed using the new classification.

Methodology

One hundred and thirty-two cases of intracranial tumors affecting children 15 years of age or younger were retrieved from pathology files at the Institute of Pathology and the King Chulalongkorn Memorial Hospital diagnosed between August 2001 and December 2004. All materials were reviewed and classified according to the recent World Health Organization classification (WHO) of nervous system tumors.[7] Recurrent tumors and lesions primarily affecting the cranial vault were excluded. Clinical correlation (with neuroimaging study and/or intraoperative findings) and immunohistochemical study were done when the conventional stain did not provide definite diagnosis.

Results

Of the 132 cases, boys were more commonly affected by brain tumors compared to girls with a ratio of 2 :1. The mean age was 7.89 years, and the distribution of tumors according to age was shown in figure 1. Table 1 summarized the histologic subtypes of tumors, the most common of which belonged to the neuroepithelial category (69.0%) such as astrocytomas of various subtypes (25.0%), ependymal tumors (18.9%), and embryonal tumors (14.4%). Germ cell tumors constituted 12.9 percent of the series. Although relatively uncommon, several tumor entities previously undocumented in the Thai series[3,4] of brain tumors were presented in this current study. These included 5 subependymal giant cell astrocytomas (SEGAs), 3 dysembryoplastic neuroepithelial tumors (DNTs), 2 AT/RTs (atypical teratoid/rhabdoid tumors), 1 pleomorphic xanthoastrocytoma (PXA), 1 desmoplastic infantile ganglioglioma (DIG), and 1 low grade hypothalamic neuronal tumor.

Tumors frequently arose in the supratentorium (81 cases, 61.4%), compared to the infratentorium (51 cases, 38.6%) with a ratio of 1.6: 1. The topographic distribution of 132

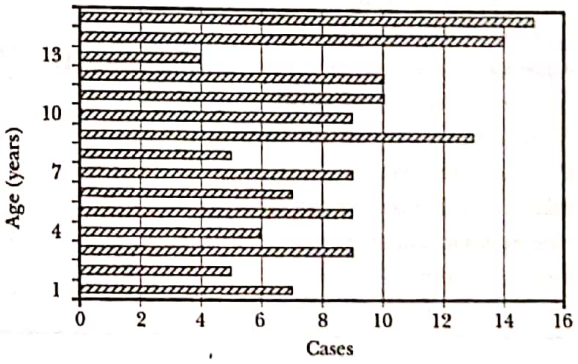

Figure 1 Age distribution of 132 childhood brain tumors

Table 1 Histologic subtype of 132 brain tumors in childhood

Types	Cases	Percent
Astrocytoma	33	25.0
Circumscribed	21	
Pilocytic astrocytoma (grade I)	5	
Subependymal giant cell astrocytoma (SEGA) (grade I)	1	
Pleomorphic xanthoastrocytoma (PXA) (grade II)*		
Diffuse	3	
Glioblastoma (GBM) (grade IV)	2	
Low grade diffuse astroctyoma (grade II)	1	
Anaplastic astroctyoma (grade III)		
Ependymal tumors	25	18.9
Ependymoma (grade II)	17	
Anaplastic ependymoma (grade III)	8	
Embryonal tumors	19	14.4
Medulloblastoma (grade IV)	15	11.4
Primitive neuroectodernal tumor (PNET) (grade IV)	2	
Atypical teratoid/rhabdoid tumor (AT/RT) (grade IV)**	2	
Neuronal and mixed neuronal-glial tumors	10	7.6
Ganglioglioma (grade I/II)	4	
Dysembryoplastic neuroepithelial tumor (DNET) (grade I)*	3	
Anaplastic ganglioglioma (grade III)	1	
Desmoplastic infantile ganglioglioma (DIG) (grade I)*	1	
Low grade hypothalamic neuronal tumor***	1	
Choroid plexus tumors	2	1.5
Choroid plexus papilloma (grade I)	1	
Choroid plexus carcinoma (grade III)	1	
Oligodendroglial tumors	1	0.8
Oligodendroglioma (grade II)	1	
Glial tumors of uncertain histogenesis	1	0.8
Gliomatosis cerebri (grade III)	1	
Germ cell tumors	17	12.9
Mixed germ cell tumor	7	
Germinoma	5	
Endodermal sinus tumor	2	
Immature teratoma	2	
Choriocarcinoma	1	
Adamantinomatous craniopharyngioma (grade I)	11	8.3
Langerhans cell histiocytosis	4	3.0
Neurilemmoma (grade I)	3	2.3
Pituitary adenoma	3	2.3
Mixed neurilemmoma and meningioma**	1	0.8
Hemangioblastoma (grade I)	1	0.8
Metastatic retinoblastoma	1	0.8
Total	**132**	**100**

**These entities were introduced in WHO 1993 and remained in WHO 2000*
***This entity was introduced in WHO 2000*
****This entity has not previously been described elsewhere to affect the hypothalamus*
*****Clinically neurofibromatosis type 2*

Table 2 Topographic distribution of 132 brain tumors in childhood

Location	Cases	Overall (%)	% according to Site
Supratentorium (81 cases)			
Cerebral hemisphere	22	16.7	100.0
Ependymoma	3		13.6
DNET	3		13.6
Anaplastic ependymoma	2		9.1
Low grade diffuse astrocytoma	2		9.1
Ganglioglioma	2		9.1
Pilocytic astrocytoma	2		9.1
PNET	2		9.1
Anaplastic ganglioglioma	1		4.6
PXA	1		4.6
DIG	1		4.6
Oligodendroglioma	1		4.6
Gliomatosis cerebri	1		4.6
AT/RT	1		4.6
Sellar-suprasellar	31	23.5	100.0
Adamantiomatous craniopharyngioma	11		35.5
Pilocytic astrocytoma	8		25.8
Langerhans cell histiocytosis	3		9.7
Mixed germ cell tumor	3		9.7
Pituitary adenoma	3		9.7
Ganglioglioma	1		3.2
Endodermal sinus tumor	1		3.2
Metastatic retinoblastoma	1		3.2
Basal ganglia	2	1.5	100.0
Germinoma	2		100.0
Thalamus-hypothalamus	8	6.1	100.0
Pilocytic astrocytoma	3		37.5
Anaplastic astrocytoma and GBM	2		25.0
Germinoma	1		12.5
Langerhans cell histiocytosis	1		12.5
Low grade hypothalamic neuronal tumor	1		12.5
Pineal region	10	7.6	100.0
Mixed germ cell tumor	4		40.0
Germ cell tumor	5		50.0
Ependymoma	1		10.0
Ventricles (excluding 4th ventricle)	8	6.1	100.0
SEGA	5		62.5
Choroid plexus tumors	2		25.0
Ganglioglioma	1		12.5
Infratentorium (51 cases)			
Posterior fossa (including 4th ventricle)	45	34.1	100.0
Medulloblastoma	15		33.3
Ependymoma	14		31.1
Anaplastic ependymoma	5		11.1
Pilocytic astrocytoma	8		17.8
AT/RT	1		2.2
Immature teratoma	1		2.2
Hemangioblastoma	1		2.2
Cerebellopontine angle	4	3.0	100.0
Neurilemmoma	3		75.0
Mixed neurilemmoma and meningioma	1		25.0
Pons	2	1.5	100.0
GBM	2		100.0

brain tumors was shown in Table 2. Posterior fossa was the most frequent site of tumors (34.1%), and ependymal neoplasms constituted 42.2 percent of lesions in this anatomical site. Thirty-one tumors (23.5%) involved the sella and suprasellar region; craniopharyngioma and pilocytic astrocytoma represented the two commonest tumors in this location. The cerebral hemispheres hosted 22 tumors (16.6 %).

Discussion

To the best of our knowledge, this is the first series of pediatric brain tumors in Thailand classified according to the recent WHO classification.[7] In parallel with most of the previously-published data including the meta-analysis of 10,582 cases, pediatric brain tumors show male predilection.[4,8,9] In most studies, the infratentorium is generally slightly more affected than the supratentorium.[4,8,10] However, the reverse ratio is observed in our present study, as well as that of Wong et al.[11] Neuroepithelial tumors are by far the most frequently-occurring brain tumors in children although an incidence of subtypes varies from series to series.[3,4,8-11] Astrocytic tumors appear to be the most common subtype of neuroepithelial neoplasms in nearly all series, including the present one. While the incidence of ependymal tumors in most studies is approximately 10 percent,[3,8,9] they constitute 18.9 percent in this study. An incidence of embryonal tumors (14.4%) in the current cohort is slightly lower than that of the published data (15.5-22.2%).[3,4,8-10] The frequency of germ cell tumor (12.9%) is higher than that of the others, but is comparable to the previous report from Thailand and other Asian countries such as Taiwan.[4,11] Craniopharyngioma makes up 8.3 percent of this reported series, which is within the ranges of previou reports.[8,11] Topographic distribution of tumor in this series is similar to that of the literature For example, medulloblastoma and ependyma tumors are common neoplasms of the posterio fossa, and the majority of pineal region tumor are those of germ cell.

It is of interest to note that, although the current series of pediatric brain tumors does no differ significantly from other recent series using the same classification scheme,[8-10] several tumor entities not previously documented in the previous studies in Thailand[3,4] have emerged in our present analysis. These include SEGA, DNT, AT/RT, PXA, DIG, and low-grade hypothalamic neuronal tumor. All except the last one have been well-described in the recent WHO classification.[7] The low grade hypothalamic neuronal tumor is an exceptional case, which to date has not been reported in the literature (manuscript in preparation). Although these entities can be viewed as uncommon tumors of the central nervous system, clinicians and pathologists must be familiar with them. Failure to recognize such entities will result in erroneous diagnoses and improper management.

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บทคัดย่อ **เนื้องอกสมองในเด็ก: การศึกษาผู้ป่วยจำนวน ๑๓๒ ราย โดยใช้การจำแนกชนิดขององค์การอนามัยโลกปี ๒๕๔๓**

สมฤทัย ช่วงโชติ*, ชนพ ช่วงโชติ**

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วารสารวิชาการสาธารณสุข ๒๕๔๙; ๑๕:๑๘๖-๙๑.

เนื้องอกของสมองเป็นเนื้องอกที่พบได้บ่อยชนิดหนึ่งในเด็ก คณะผู้วิจัยได้รายงานผู้ป่วยเด็กที่มีอายุน้อยกว่าหรือเท่ากับ ๑๕ ปี จำนวน ๑๓๒ รายที่เป็นเนื้องอกสมอง ผู้ป่วยทั้งหมดได้รับการวินิจฉัยระหว่างเดือนสิงหาคม พ.ศ. ๒๕๔๔ ถึงเดือนธันวาคม พ.ศ. ๒๕๔๗ ที่สถาบันพยาธิวิทยา กรมการแพทย์ และภาควิชาพยาธิวิทยา คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย โดยใช้เกณฑ์การจำแนกชนิดขององค์การอนามัยโลกปี ๒๕๔๓ การศึกษา พบจำนวนผู้ป่วยเด็กชายเป็นสองเท่าของผู้ป่วยเด็กหญิง อายุเฉลี่ยของผู้ป่วยโดยรวมเท่ากับ ๗.๘๕ ปี รอยโรคพบบ่อยใน supratentorium เมื่อเทียบกับ infratentorium ในอัตราส่วน ๑.๖ ต่อ ๑ เนื้องอก neuroepithelial จัดเป็นเนื้องอกที่พบได้บ่อยที่สุด เช่น astrocytoma (๒๕.๐%), ependymoma (๑๘.๕%) และ embryonal tumors (๑๔.๔%) อัตราอุบัติการของเนื้องอกชนิด germ cell tumors (๑๒.๕%) ใกล้เคียงกับที่มีรายงานในประเทศแถบเอเชีย ซึ่งพบว่าสูงกว่าที่มีรายงานในประเทศทางตะวันตก เนื้องอกที่พบบ่อยใน infratentorium ได้แก่ ependymal neoplasms (๑๔.๔%), medulloblastoma (๑๑.๔%) และ pilocytic astrocytoma (๖.๑%) การศึกษานี้พบเนื้องอกหลายชนิดที่ไม่เคยตรวจพบมาก่อนในอนุกรมการศึกษาเนื้องอกสมองของประเทศไทย ซึ่งได้แก่ subependymal giant cell astrocytoma (๕ ราย), dysembryoplastic neuroepithelial tumor (๓ ราย), atypical teratoid/rhabdoid tumor (๒ ราย), pleomorphic xanthoastrocytoma (๑ ราย), desmoplastic infantile ganglioglioma (๑ ราย) และ low grade hypothalamic neuronal tumor (๑ ราย) การตระหนักถึงเนื้องอกชนิดใหม่ ๆ เหล่านี้มีความสำคัญต่อการวินิจฉัย อันจะนำไปสู่การรักษาผู้ป่วยที่เหมาะสม

คำสำคัญ: **เนื้องอกสมอง, เด็ก, การจำแนกชนิดตามองค์การอนามัยโลก**