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## Epidemiology of pediatric tumors of the nervous system according to the WHO 2000 classification: a report of 1,195 cases from a single institution

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**Abstract** *Object:* The purpose of this study is to determine the epidemiology of tumors of the nervous system diagnosed according to the WHO 2000 classification in a single Brazilian institution. *Patients and method:* One thousand one hundred ninety-five tumors in children between 0 and 21 years of age diagnosed between 1974 and 2003 were classified according to the sex, topography, and age distribution. *Results:* In all ages, males were slightly more affected. In the first 2 years, the prevalence for boys was higher (68.3%). In the whole series, 58.7% were supratentorial, 31.4% infratentorial, and 9.9% spinal (44% intra- and 56% extramedullary). Among these latter, ependymomas and schwannomas were the most frequent. In the cerebral compartment, pilocytic astrocytomas were the single most frequent tumors (18%), followed by diffuse astrocytomas (14%), medulloblastomas (11%), and cranio-pharyngiomas (11%). In the posterior fossa, there was an even distribution

among pilocytic astrocytomas, but the former was much more frequent in the first 2 years of age. High-grade (III and IV) diffuse astrocytomas were slightly more frequent than low grades (II), and this difference becomes more evident as the child grows older. Due to the new development of the surgery of epilepsy, the frequency of neuronal and mixed neuronal–glial tumors is increasing (8%). *Conclusion:* Classified according to the latest WHO classification, by a single neuropathologist in a single institution, this large series of pediatric neurological tumors may reflect fairly well their real incidence. Our results obtained in a developing country do not differ substantially from other similar series reported in the literature from the First World.

**Keywords** Pediatric tumors of the nervous system · Epidemiology · WHO classification of tumors

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### Introduction

Tumors of the nervous system are the second commonest type of neoplasia of childhood after leukemia. The annual incidence varies between 1.7 and 4.1/100,000 children, and it seems that there is a slight increase in annual incidence for the last two decades [3, 5, 16]. In the USA, it is esti-

mated that 2,200 children develop nervous system tumors each year [1]. Albeit the progress in early detection, surgical procedures, and therapeutic strategies, the overall prognosis of these tumors remains poor. In a recent study from the USA [2], only 33% of the patients were alive at follow-up 5 years after surgery. However, there are conspicuous differences as to prognosis among the nervous

system neoplasms either according to the different histological types or their topography.

There are several reports regarding the epidemiology of tumors of the nervous system in children. However, most are based on population-based or institutional tumor registries [3, 7–9]. The major flaw of such studies concerns the fact that different classification schemes may have been adopted by the several institutions from which the data are taken. Also, two other issues concerning astrocytic tumors and medulloblastomas, which are the most frequent pediatric tumors, need to be clarified. In several reports, the former is taken as a whole, and medulloblastomas and primitive neuroectodermal tumors (PNETs) are considered the same type of neoplasm [14, 15, 17]. Actually, astrocytic tumors are a heterogeneous group of neoplasms with distinct biological behavior varying from grade I (pilocytic astrocytomas) to grade IV (glioblastoma multiforme) of malignancy. These different types of astrocytomas constitute distinct clinicopathological entities that must be individualized in the schemes dealing with these issues. As to the medulloblastoma/PNET issue, the current view of most neuropathologists including the WHO classification of tumors of the nervous system [4] considers these neoplasms as distinct entities whose propensity to occur in various sites within the neuroaxis, and the response to treatment is quite different. As with the astrocytic tumors, these neoplasms must appear under different headings in order to allow the actual detection of their incidence.

The present study is an epidemiological analysis of 1,195 consecutive tumors of the nervous system whose anatomopathological diagnosis was performed in a single institution by a single neuropathologist. It is worth mentioning that to our knowledge, this is the only study of this kind performed in a developing country so that it will be possible to compare the epidemiology of the pediatric tumors of the nervous system between different socioeconomic populations.

## Patients and methods

One thousand one hundred ninety-five consecutive tumors of the nervous system in children from 0 to 21 years of age histologically diagnosed at the Division of Pathology of the Hospital das Clínicas of the São Paulo University School of Medicine between January 1974 and December 2003 were reviewed. In some cases, mainly in those whose diagnosis had been performed prior to the immunohistochemistry era, the initial diagnosis was remade with the utilization of this technique. Also, in 1998, a special cohort of tumors including embryonal and low-grade gliomas was reviewed in order to detect the recently recognized dysembryoplastic neuroepithelial tumor (DNT) [13]. The tumors were classified and graded according the WHO 2000 scheme [4]. Other recently described entities not yet contemplated in this classification were included.

**Table 1** Histologic types of spinal tumors

Histologic types of spinal tumors	n=116	Percent
Astrocytoma (II)	11	9.5
Anaplastic astrocytoma (III)	4	3.4
GBM (IV)	1	0.9
Pilocytic astrocytoma	13	11.2
Ependymoma	14	12.1
PNET	8	6.9
Ganglioglioma	5	4.3
Peripheral nerve sheath tumors	21	18.1
Epidermoid cyst	4	3.4
Meningioma	3	2.6
Lymphoma	7	6.0
Lipoma	7	6.0
Others	18	15.5

*GBM* Glioblastoma multiforme

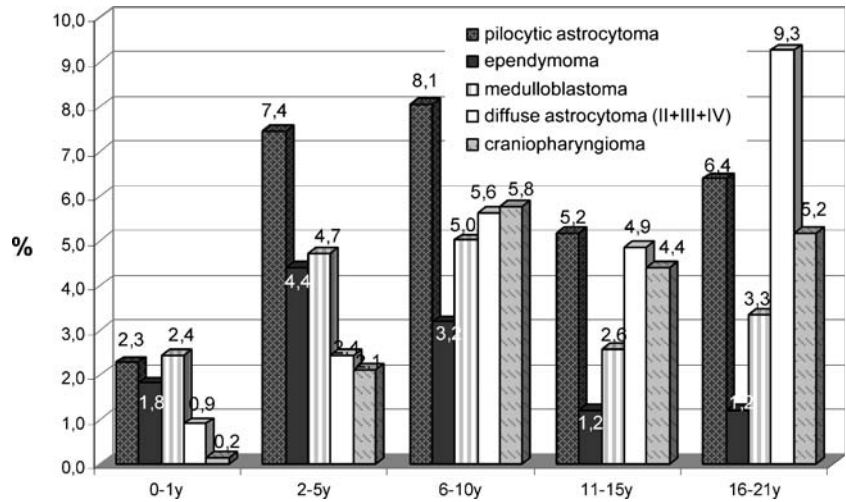
## Results

According to the gender, 54% of the tumors occurred in males and 46% in females. Of the tumors, 58.7% were situated in the supratentorial (ST) compartment, 31.4% in the infratentorial (IT), and 9.9% in spinal canal (SC). However, in the first 2 years of life (104 cases), 68.3% of

**Table 2** Histologic types of brain tumors

Histologic types of brain tumors	n=1,058	Percent
Astrocytoma (II)	66	6.2
Anaplastic astrocytoma (III)	47	4.4
GBM (IV)	39	3.7
Pilocytic astrocytoma	193	18.2
Ependymoma	78	7.4
Oligodendroglioma	10	0.9
Choroid plexus tumors	32	3.0
Mixed neuronal and neuroglial tumors	80	7.6
Hypothalamic hamartoma	4	5
Gangliocytoma	13	16
Ganglioglioma	39	49
Desmoplastic infantile astrocytoma	3	4
Ganglioneuroblastoma	3	4
Ganglioneurocytoma	1	1
Central neurocytoma	3	4
DNT	14	17
Medulloblastoma	119	11.2
PNET	29	2.7
Meningioma	32	3.0
Pituitary adenoma	60	5.7
Craniopharyngioma	116	11.0
Germ cell tumors	38	3.6
Other	119	11.2

**Fig. 1** Distribution of the five most frequent tumors in relation to age



the affected children were males. Fifty-eight cases (55.7%) were ST, 33 (31,8%) were IT, and 13 (12.5%) were spinal.

The histologic types of the spinal tumors are listed in Table 1. Of these, 44% were intramedullary (ependymoma being the most frequent tumor) and 56% were extramedullary, intra- or extradural. Peripheral nerve sheath tumors (mostly schwannomas) were by far the most frequent tumors of this region.

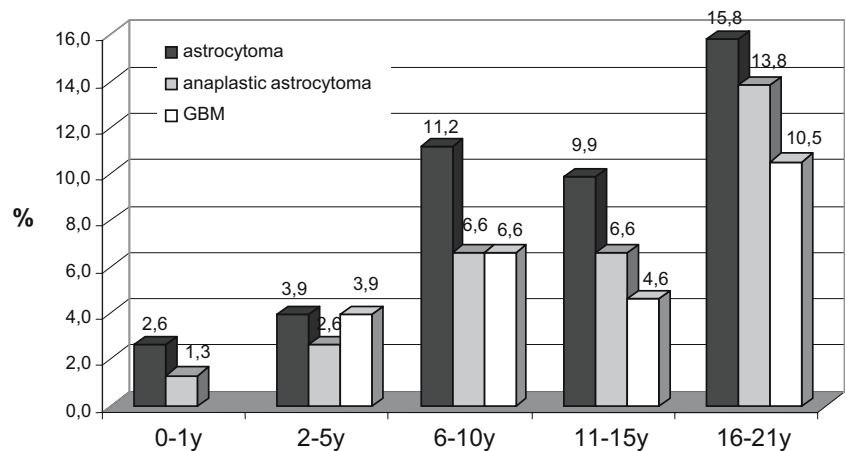
The histological types of the brain (intracranial) tumors are listed in Table 2. The topographic distribution plotted with the histological types were as follows: *hemispheric*=24.4% (diffuse astrocytomas=34.9%, ganglioglioma/gangliocytoma=16.7%, pilocytic astrocytoma=11.6%, DNT=5.4%, meningioma=6.6%, others=24.8%); *lateral ventricles*=7.8% (choroid plexus tumors=32.9%, ependymoma=23.2%, subependymal giant cell astrocytoma=14.6%, others=29.3%); *basal ganglia/thalami*=3.9% (diffuse astrocytomas=53.7%, pilocytic astrocytoma=22%, others=24.3%); *selar*=19% (craniopharyngioma=57.7%, pituitary adenoma=29.8%, germinoma=5.5%, others 6.9%); *pineal region*=3.3% (germinoma=25.7%, pineocytoma/pineoblastoma=

20%, teratomas=14.3%, others=40%); *hypothalamus/optic pathways*=4.3% (pilocytic astrocytoma=89.1%, ganglionic hypothalamic hamartoma=10%); *cerebellum/IV ventricle*=30.9% (medulloblastoma=36.4%, pilocytic astrocytoma=31.5% ependymoma=17.4%, others=14.7%); *brain stem*=2.3% (diffuse astrocytomas=66.7%, pilocytic astrocytoma=16.7, others=16.6%); and *base of the skull*=4.1% (chordoma=18.6%, epidermoid cysts=7%, schwannoma=51.2%, others=23.3%).

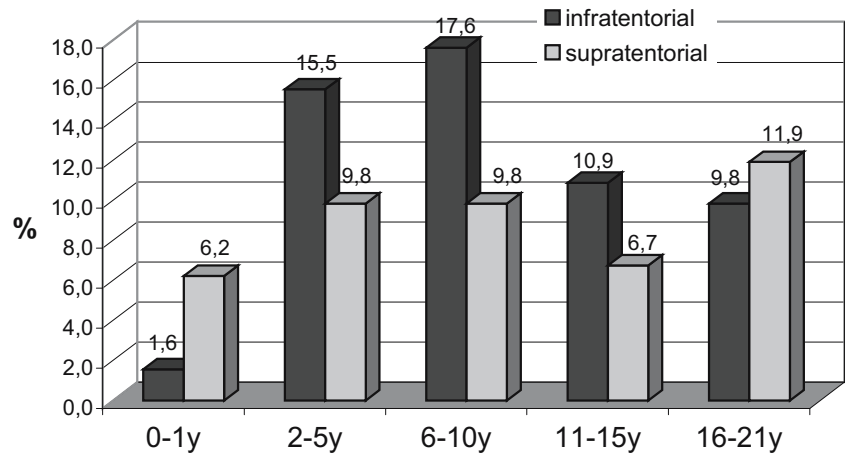
According to their topography, the distribution of the main tumors was as follows: pilocytic astrocytoma (ST=41.8%, IT=51.9%, SC=6.3%), diffuse astrocytoma (ST=72%, IT=18.5%, SC=9.5%), ependymoma (ST=26.5%, IT=58.2%, SC=15.3%), ganglioglioma/gangliocytoma (ST=86%, IT=5.2%, SC=8.8%), choroid plexus tumors (ST=84.4%, IT=15.6%).

Figure 1 represents the distribution of the most frequent tumors through the patient's ages. The distribution of the three types of diffuse astrocytomas, pilocytic astrocytoma, and ependymoma, as well as the cerebellar/IV ventricle tumors according to age, is shown in Figs. 2, 3, 4, 5.

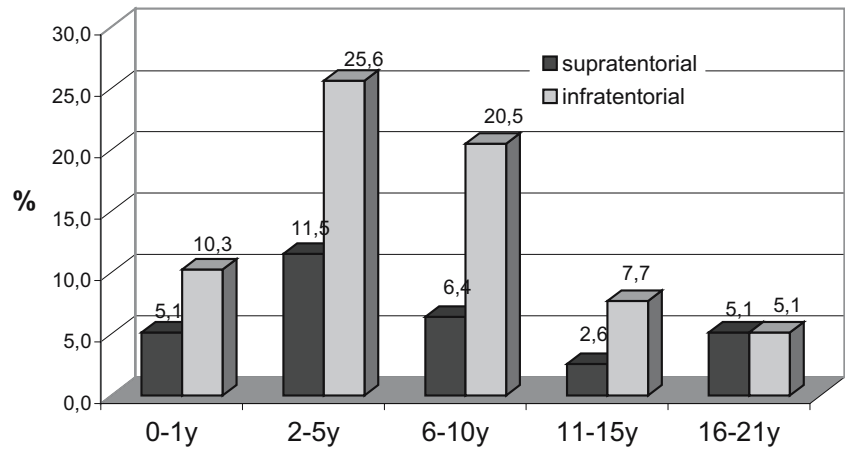
**Fig. 2** Distribution of diffuse astrocytomas in relation to age



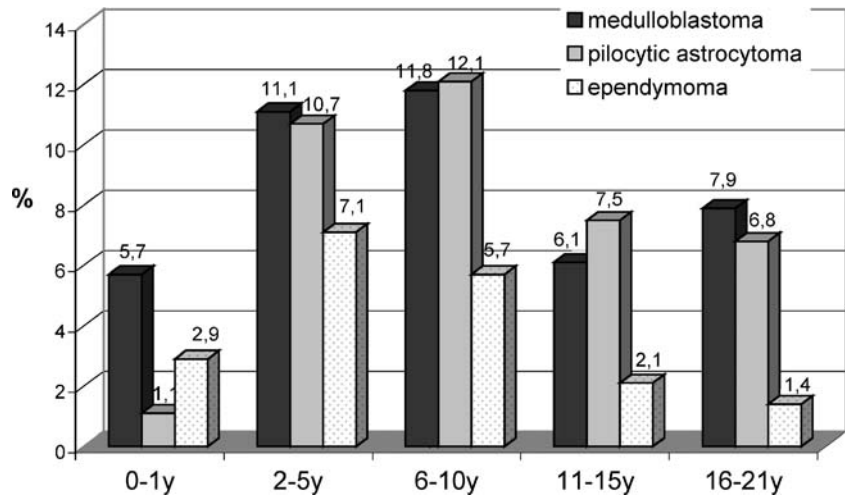
**Fig. 3** Distribution of pilocytic astrocytomas according to topography and in relation to age



**Fig. 4** Distribution of ependymomas according to topography and in relation to age



**Fig. 5** Distribution of cerebellar and IV ventricle tumors in relation to age



**Discussion**

We think that our results reflect fairly well the incidence of tumors of the nervous system in childhood due to the fact that this study was performed through many years in a

single institution with a homogeneous neuropathological approach. They do not differ substantially when compared with those of most series reported in the literature in which the methodology was similar to ours [11, 12].

In general, males are slightly more affected than females. However, in the first 2 years of life and between 2 and 5 years, respectively, about 68% and 60% of the cases occur in males.

It is commonly stated that in children, the tumors of the posterior fossa are more frequent than those arisen in the ST compartment. However, when reviews of population-based and institutional tumor registries are taken together [8, 9], it emerges that there is an even distribution among infra and ST tumors and, in some series, like ours, there is a predominance of the latter. This is particularly true when one considers the tumors in the first 2 years of life. At this period, 64% of the 91 intracranial tumors found in our series were situated in the ST compartment. However, the actual incidence of the tumors of the posterior fossa may be slightly higher than shown in our series because the majority of the brain stem tumors (glioma of the pons) are not biopsied. We estimate that these tumors represent 10 to 20% of those situated in the posterior fossa.

In the cerebellum, medulloblastomas and pilocytic astrocytomas are almost evenly distributed. However, in the first 2 years, the former is more frequent.

Pilocytic astrocytoma is the most frequent tumor of the nervous system in children performing almost one fifth of all neoplasms. More than half of them are cerebellar and they represent the vast majority of the tumors of the optic/hypothalamic region, almost one third of the cerebellar/IV ventricle, one fourth of the basal ganglia/thalamic, and 11% of the hemispheric tumors. Diffuse astrocytomas that are by far the most frequent tumor of the nervous system in

adults represent almost 15% of all tumors in children. It is worth mentioning that high-grade tumors (grades III and IV) are as frequent as low-grade (grade II) tumors. Almost 90% of them are situated in the cerebral hemispheres or in the basal ganglia/thalamic region.

Due to the recent development of surgery of epilepsy techniques, neuronal and mixed neuronal–glial tumors perform a quite high percentage (8%) of the brain tumors in our series. The majority of these tumors are represented by gangliogliomas, gangliocytomas, and DNTs, which commonly lead to chronic intractable epilepsy.

Tumors recognized in the last quarter of the century are indeed very rare, DNT being the most frequent of them ( $n=14$ ). The others included pleomorphic xanthoastrocytoma ( $n=6$ ), atypical teratoid/rhabdoid tumor ( $n=3$ ), desmoplastic infantile astrocytoma ( $n=3$ ), and central neurocytoma ( $n=3$ ). Cerebellar liponeurocytoma, choroid, and rhabdoid meningiomas have not been diagnosed. Other rare entities [6, 10] not yet contemplated in the WHO 2000 scheme are the ganglioneurocytoma, the ganglioneuroblastoma, and the papillary glioneuronal tumor. We found, respectively, 1, 3, and 0 cases of such tumors in our series.

We think that these data may reflect the real epidemiological status of pediatric brain tumors and that the incidence of these neoplasms in a developing country does not differ substantially from that found in first-world countries. This is another argument speaking against a possible role of environmental factors in the genesis of tumors of the nervous system.

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