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CHILDREN AGED 0-15 YEARS BRAIN TUMOR: EPIDEMIOLOGY, CLINIC, THERAPY AND PROGNOSTIC IN YAOUNDE-CAMEROON

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ABSTRACT

Brain tumor is the second most frequent childhood solid tumor after leukemia. Neurosurgery remains the first outcome for biopsy as well as for anatomic pathology evaluation purposes for therapeutic resections. This study was a longitudinal descriptive design with a retrospective (10 years) and prospective (6 months) study periods. The study general objective was to appreciate and describe the epidemiological, clinical, therapeutic aspects of childhood brain tumor so as to define a prognostic profile of these tumors. 68 cases of brain tumor constituted our sample size. Patients' clinical presentation at diagnosis was dominated by the intracranial hypertension syndrome (80.4%). Presumptive diagnosis after brain scanner was dominated by astrocytoma (47.8%), followed by medulloblastoma (8.7%) and glioma (6.5%). Only 5% of the children underwent chemotherapy and just 1 patient radiotherapy. These were the only therapeutic modalities after neurosurgery whereby all the other children went through. The rate of mortality after surgery in this study was 21.7%.

Key Words: brain tumor, chemotherapy, childhood, radiotherapy, neurosurgery

I- INTRODUCTION

Brain tumors are groups of intracranial neoformations, be it intra or extra axial as point of origin. In children, they result from the period of neonatal life to adolescence and constitute the most common solid tumor and leading cause at this age [1,2], with an incidence rate estimated at 2.5 to 4 cases per 100 000 habitants annually, making it the second leading cause of cancer death in children after leukemia in Europe [3]. Clinical diagnosis is particularly very difficult in new born babies whereby irritability, apathy, vomiting's, weight loss or epilepsy give other etiological orientations. In children, signs of intracranial hypertension may be the only present signs for a long period of time (headache, vomiting…), neurological signs do appears only late as such, in favor of a late diagnosis [1,4,5]. Therapeutic management is liable to the histological and topographic nature of the tumor and the age of the child. It calls on surgery, radiotherapy and chemotherapy. That is why, the therapeutic decision relies on the confrontations between neurosurgeons and pediatric oncologists [6,7]. Several survivors of these tumors suffers from chronic sequelae as direct consequence of the tumor and treatment outcomes. Moreover, these patients are at high risks of presenting secondary malignant tumors [6]. Yet, limited or no study about the treatment and prognostic of these childhood brain tumor is known in Cameroon. As such, we found it innovative to carry out such a study on the epidemiological, clinical, therapeutic and prognostic characteristics of childhood brain tumors at the "Centre Mère et Enfant de la Fondation Chantal Biya" and the Yaoundé Central Hospital so as to define the prognostic profile of Childhood brain tumor in Yaoundé-Cameroon.

II- METHODOLOGY

1- Study design and setting

The design was a longitudinal descriptive, prospective and retrospective study carried out at the Yaoundé Central Hospital and "Centre Mère et Enfant de la Fondation Chantal Biya" going from the period of November 30th 2005 to November

30th 2015 either a period of 10 years as for the retrospective part of study and from December 1st 2015 to May 31st 2015, was the prospective period of study either 6 months.

2- Study subject and method

Our population of study concerned children of both sex (male and female) aged between 0 and 15 years where a brain tumor was diagnosed and taken in charge in the above hospitals. Were included as such to the retrospective part of the study all the available exploitable medical file of children diagnosed with a brain tumor and for the prospective part of study, all the children whose parents consented to take part to the study were included. On the other hand, children with secondary brain tumors and an intracranial expansive non tumoral process, with non-consented patients were excluded from study.

3- Statistical data analysis

Collected data were recorded by the software CSPRO Version 6.0 and analyzed using the software SPSS. Quantitative data were presented in terms of means, standard deviation and percentages. Qualitative data were presented in terms of numbers and frequencies. For comparison of proportions, the khi square test was used when the variable had more than two modalities. When the number of a modality was less than 5, we used the Fisher Exact test. Results were considered statistically significant if p value less than 0.05 pour a confidence interval of 95%. We used equally the graph of Kaplan Meier to evaluate survival.

III- RESULTS

1- Sociodemographic data

68 children took part to the study amongst which 38 of them were male (55.9%) and 30 female (44.1%). The mean age of the sample was 8.42±4.2 years with extremes at 10 months and 15 years. The most represented age group was that of 8 and 13 years with a rate of 35.3%, followed by those of 5 to 8 years and 13 to 16 years with 22.1%

both. In the population of boys as well as girls, we observe two peak values: first, between the ages of 8 to 13 years and between 13 to 15 years for boys and secondly for girls, between 5 to 8 years and 8 to 13 years as shown in fig1 below.

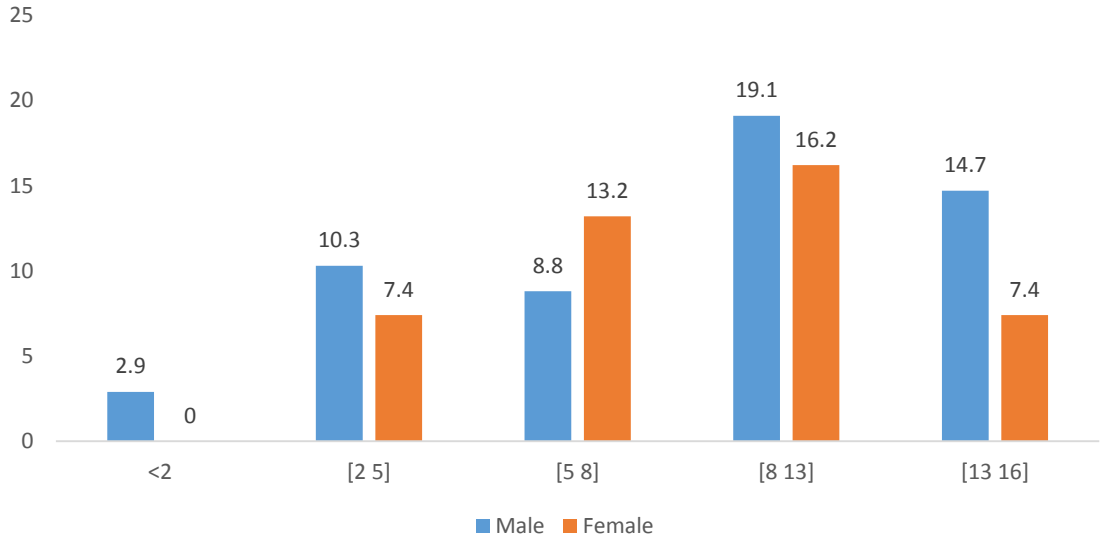

Figure1: Distribution following age and sex

2- Clinical data

a) Clinical representation

Clinical presentations during consultations which permitted to carry out diagnosis was dominated by intracranial hypertension (80.4%), followed by a symptomatology of cranial nerve involvement (43.5%), cerebellar syndrome (39.1%), seizures (28.3%) and lastly hemi-body deficit (26.1%).

Table1: Clinical Representation

Clinical Manifestations	Numbers (n)	Percentages (%)
Intracranial hypertension	37	80,4
Cerebellar Syndrome	18	39,1
Hemi-corporal deficiency	12	26,1
Blindness	3	6,5
Seizure	13	28,3
Higher brain functions damage	9	19,6
Cranial nerve involvement	20	43,5

b) Symptoms following localization

Headaches was the major symptom independent of any localization of the tumor. It was present in 76% of supratentorial lesions and 71.4% in sub temporal lesions. The second most frequent symptom was vomiting which was the main characteristic symptom of sub temporal lesions in 73.3% against 26.7% for supratentorial lesions. Cranial nerve involvement was equally distributed between sub temporal 44% and supratentorial in 47.7%.

Table 2: Signs and Symptoms

Clinical signs	**Supratentorial lesions**	Sub-temporal lesions
	N (%)	N (%)
Headache	15 (71,42)	19 (76)
Vomitings	8 (38,1)	22 (88)
Macrocranium	2 (9,5)	1 (4)
Blurred vision	8 (38,1)	9 (36)
Blindness	3 (14,3)	1 (4)
Seizure	7 (33,3)	6 (24)
Altered level of consciousness	5 (23,8)	4 (16)
Cranial nerve involvement	10 (47,7)	11 (44)
Dysphasia	2 (9,5)	0

N=number and %=Percentage

3- Para clinical data

Informations concerning brain scanner of 46 patients were obtained and confirmation of the tumor by anatomic pathology obtained from 34 patients.

a) Tumor localization

The posterior cerebral fossa contained 54.3% of the whole tumors while 45.7% of the tumors were located in the supratentorial region and 15.2% in the sub temporal region. The tumors of the supratentorial region were mostly located in the cerebral hemispheres in 42.9%, then by the intra axial in 38.1%. The tumors of the sub

temporal region were mainly located in the cerebral vermis (46.1%), the cerebral hemispheres (30.8%) and the fourth ventricle (11.5%) as shown in the table below.

Table 3: Supratentorial and Sub Temporal localizations

Distributions	Number (n)	Percentage (%)
Sub temporal (n=25)		
Cerebral hemispheres	8	30,8
Brain stem	2	7,7
Cerebellar vermis	12	46,1
Cerebellopontine angle	1	3,8
4th ventricule	3	11,5
Supratentorial (n=21)		
Cerebral hemisphere	9	42,9
Intra-axial	8	38,1
Extra-axial	2	9,5
Intraventricular	2	9,5

b) Presumptive diagnosis after brain scanner

After a brain scanner, we establish a presumptive diagnosis. 47.8 % pilocytic astrocytoma, 8.7% medulloblastoma, 6.5% glioma and 4.3% meningioma.

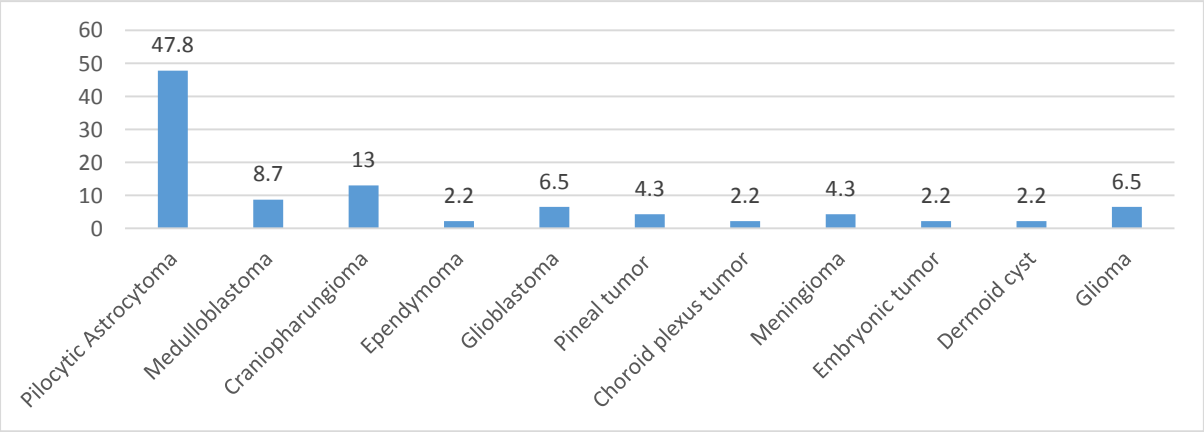

Figure 2 : Presumptive Scanographic Diagnosis

c) Scannographic associated signs

Hydrocephalus is the most represented Scannographic sign with 63%. Encystment follows with 47.7%. Calcifications were observed in 17.4% of the patients. Lesions of the posterior cerebral fossa represented 62.1% of hydrocephalus and 37.9% responsible for supratentorial tumors. Among the tumors of the posterior fossa, those of vermis localization represented 44.4% of hydrocephalus while hemispheric tumors represented 33.3% and the fourth ventricle 16.7%.

d) Histological profile

The histology of the tumors was obtained among 34 patients. Pilocytic astrocytoma predominated with 41.2%. Medulloblastoma counted for 17.2%, ependymoma counted for 8.8% and glioblastoma counted for 5.9%. Pilocytic astrocytoma is the most represented histological type present in the lesions of the posterior cerebral fossa with 52.6% followed by medulloblastoma with 31.6%. In the sub temporal region, astrocytoma remains the most spread type with 26.7%.

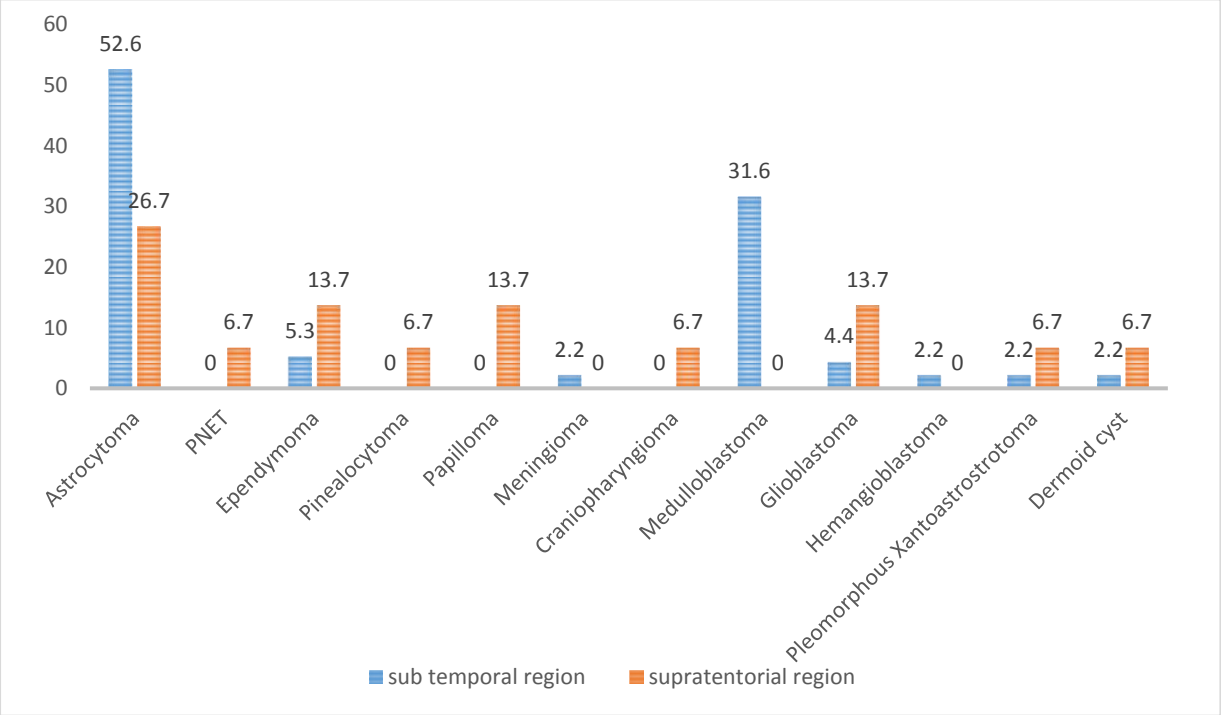

Figure 3 : Proportions of histological types

4- Treatment

Exclusive neurosurgical treatment was realized within 75% of the patients. Then, radiotherapy within 12.5% of the patients

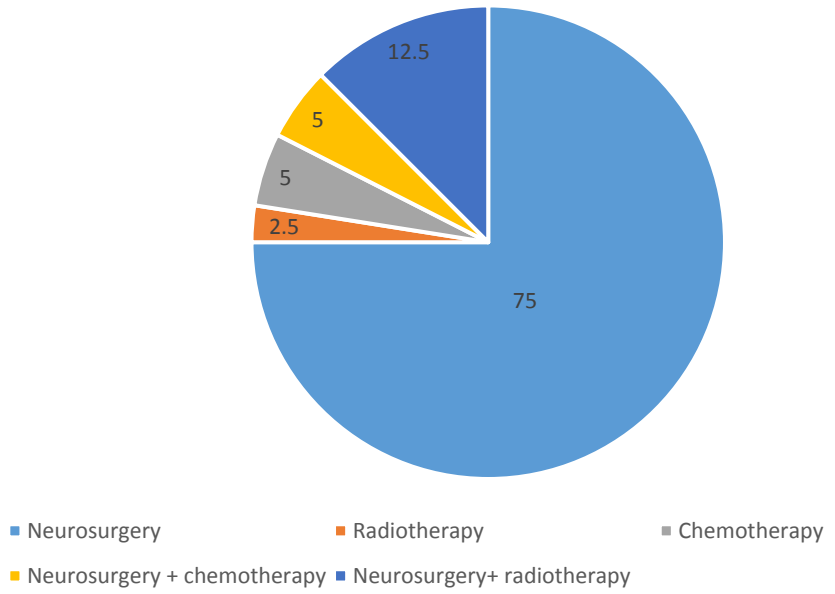

Figure 4 : Administered treatments

a) Neurosurgery

Among the operated sample, complete tumoral resection was practiced in 50% of the patients. 25% of them underwent a ventriculo-peritoneal shunt, 19.4% had a partial tumoral resection and one patient was imposed a lobectomy. 42.7% of the tumors located in the cerebral hemispheres benefited from a total resection. 66.6% partial resection was done for tumors located in the cerebral vermis.

b) Radiotherapy

Six children, either 13% of our sample underwent a radiotherapy. The radiotherapy was complementary to surgical intervention for five children. One patient underwent as unique therapeutic means radiotherapy because of its pineal tumoral localization and limited surgical plateau technique.

c) Chemotherapy

It was the adjuvant treatment to surgery for two children and unique treatment (chemotherapy) for two other children. Molecules used were: bleomycin, procarbazine, etoposide and platinum salt.

5- Evolution

Study revealed a global mortality rate of 41.3%, a survival rate of 37% and 10 lost to follow up. Post-operative mortality was 21.7%. There was no association between the localization of the tumor and post-operative mortality. There was equally no statistical association between the type of neurosurgery practiced and post-operative mortality. We found no association between the mortality rate and the histological tumoral type. 50% of the patients with astrocytoma are alive, 66.7% of those with Medulloblastoma died and the rest lost to follow-up. Among the 17 living children, 8 of them presented sequelae, 50% of them had hemiparesis for the most, and 37.5% had blindness. One child presented recidive.

IV- DISCUSSION

1- Sociodemographic characteristics

In this design study, we note a predominance of the male sex as usually found in other literatures [8,9,10]. Yet, other studies revealed the contrary of the male sex predominance and null sex dominance [3,11,12].

The mean age at diagnosis was 8.24±4.2 years, for a median of 9 years with extremes at 10 months and 15 years. This mean age approaches those of Dupuis-Girod and al.; and Odom GL and al.;[11,13]

2- Clinical data

More than 80% of the patients presented an intracranial hypertension whereby the symptomatology was dominated by headaches (73.9%), followed by vomiting (63%), blurred vision (37%) and a macro-cranium (13.5%). These obtained clinical signs are greatly described in literatures [11,14,15].

Furthermore, we obtained a statistically significant association between intracranial hypertension and supratentorial and sub temporal localization of the tumors. The high prevalence of intracranial hypertension in childhood brain tumors can be explained by its physiopathology as described by certain authors [1,14,16]

A cerebellar syndrome was found in 39.1% of the patients. It was mostly present in the tumors of the posterior fossa (53.8%) than that of the supratentorial region (23.8%). Similar results were obtained by [39] whereas Mbonda E and al.; [3] obtained 35%. On the other hand, more than 47% of the patients had a cranial nerve involvement in this study. The result is similar to that of Dupuis-Girod S and al.; [11] but less than that of Olasode B and al.;[17] who obtained a prevalence of 77% in the tumors of the brain stem.

Signs of focalization was present in 45% of the patients amongst which 21.7% manifested themselves via commissions and 26.1% by a hemi corporal deficiency.

These results approaches closely the study of Dupuis-Girod and al.;[11] but much greater than that of Petit A and al.; [18] who obtained a prevalence of 17% seizure but less than that of Mbonda E and al.;[3] who found 36.8%seizure in his study.

3- Morphological data

a) Brain scanner

46 patients had a brain scanner which permitted to determine the localization of the tumor, and following the radiographic characteristics to give a presumptive diagnosis.

Posterior cerebral fossa

It represented 54.3% of the tumors, similar remark with the results of Olasode B and al.;[17] who obtained 56.4% of lesions localized in the posterior cerebral fossa as well as that of Mbonde E and al.;[3] who obtained 54.7%. Nevertheless, certain studies obtained equal distribution of tumors between the supratentorial and sub temporal regions [13,19,20].

Supratentorial region

45.7% represented the lesions found in this region. This result is similar to those of the following authors [14,16,17]. Elsewhere, other studies found that the prevalence of tumor in the supratentorial region was greater [11,18]. Our results are similar once more to those of Tomita T and al.; [19] and Rickert CFI and al.; [21] for axial tumors but much greater for hemispheric tumors.

b) Histology

Pilocytic Astrocytoma

It represented 41.2% of the whole tumors. Obtained result is similar to those found in literatures [40,41,47]. Much lesser than those of [2,15,23] and more greater than that of Dirks PB and al.;[24].

Medulloblastoma

It stood for about 1/3 of the tumors of the supratentorial region in this study after pilocytic astrocytoma. It represented 17.6% of the tumors in the sample. These results are nearly similar to those of Dupuis-Girod and al.; [11] and Odom GL and al.;[13]

Ependymoma

It represented 8.82% of the brain tumors, corroborating with those of the following authors [3,15,17,23]. Nevertheless, certain authors do not find ependymoma in children [12,25]

Glioblastoma

Glioblastoma stood for 5.8% of the whole tumors and 13.4% of lesions situated at the supratentorial region. Obtained results are similar to that of Dupuis-Girod and al.; where they obtained 9% representation of glioblastoma in the whole sample of their study and 13.5% lesions of the supratentorial region.

Papilloma of the choroid plexus

It represented 5.8% of the tumors and 13.4% of the tumors of the supratentorial region. Obtained result is greater than that of Eyenga V-C and al.;[23] where childhood brain tumor represented just 1.1% whereas, Ezzat S and al.;[2] found 1.6% and Gjerris F [25] registered zero case of child brain tumor.

4- Treatment and evolution

Treatment

The study reveals that, 78.3% of the patients underwent neurosurgery, 12.5% adjuvant radiotherapy and 5% adjuvant chemotherapy. This low rate of use of chemotherapy and radiotherapy may be as a result of the limited or insufficient

coordination between the unit of neurosurgery and pediatric oncology that are located in two different sites.

Prognostic

We obtained a post-operative mortality rate of 21.7%. It was less than that of Mazzucco A and al.;[26] which was 36.3% and greater than that of Dupuis-Girod and al.;[11]. This difference may be as a result of diagnostic delay which was of about 140 days in this design study.

V- CONCLUSION

This design study permitted us to know that, averagely 7 cases of childhood brain tumor is diagnosed and managed every year in Yaoundé. The tumoral lesions arises frequently during the first decade of childhood with a male sex predominance. Diagnosis is delayed and most of the patients who consult presents signs of intracranial hypertension, cranial nerve involvement, cerebellar syndrome and signs of focalization. The tumors were mostly present in the posterior cerebral fossa and responsible of hydrocephalus. Brain Scanner remains the best diagnostic mean with a presumptive diagnostic confirmation from anatomic pathology. Neurosurgery was the mean of cure. The associated adjuvant treatments were radiotherapy and chemotherapy which is less practiced in our milieu. The prognostic is not good: 41.3% global mortality rate, average survival rate 22 months and survivors of neurosurgery with sequelae 47%.

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