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Intracranial tumors during the 1st year of life

Ercole Galassi, Umberto Godano, Michele Cavallo, Roberto Donati, and Maria Teresa Nasi

Division of Neurosurgery, Bellaria Hospital, Via Altura, 3, I-40139 Bologna, Italy

Abstract. Twenty-eight patients with intracranial tumors symptomatic during the 1st year of life were managed from January 1970 to March 1988. Supratentorial location (19 cases) was dominant over the infratentorial. The most common histological type was astrocytoma; choroid plexus papilloma and ependymal tumors followed in frequency. Twenty-two infants (78.6%) had associated hydrocephalus. Macrocrania, vomiting, delayed milestones, and behavioral disturbances were the chief clinical manifestations. Four patients were admitted in extremely deteriorated condition and died preoperatively. Twenty cases underwent surgery for tumor removal with a 1-month mortality rate of 20%. Tumor excision provided permanent relief of hydrocephalus in the majority of the surviving cases. Five patients received conventional radiotherapy. Stereotactic brachytherapy yielded an excellent result in 1 case. Overall 13 cases are currently alive; 6 of them have survived longer than 6 years. Fourteen of the 15 patients who were dead at follow-up succumbed within 1 year after diagnosis.

Key words: Brain neoplasm – Choroid plexus papilloma – Infant – Hydrocephalus – Neonate – Radiotherapy.

Intracranial neoplasms occurring in the 1st year of life have frequently been considered very uncommon in the past: their incidence among all brain tumors in childhood ranged between 1.4% and 5% in most of the earlier studies published [2, 14, 23, 25, 44]. In 1964 Matson [30] reported on tumors of the central nervous system (CNS) during the first 2 years of life and suggested that many of these are suitable for satisfactory surgical treatment.

The advent of neuroimaging techniques and the widespread availability of noninvasive CT examination for infants suspected of a neurological abnormality has enabled the easier and earlier detection of intracranial tumors [21, 47, 49]. Increasing numbers of intracranial tumors presenting under the age of 1 year have been reported in the recent neurosurgical literature [8, 12, 22, 26, 28, 38, 42–44, 48, 49, 51, 55]. From these articles a statistically higher representation of such entities among all pediatric brain tumors is deducible: 7.7% in the London series [22], 8% in the Buenos Aires series [55], 11% in Raimondi's experience [38], 18% and 22.5% respectively in the studies by Sakamoto et al. [42] and Locatelli et al. [28].

It is now widely accepted that CNS neoplasms at this age display such differences from these of later childhood that a separate treatise is warranted.

The purpose of this paper is to discuss some characteristic pathological, clinical, and therapeutic aspects by analyzing our experience with 28 such tumors and by reviewing the pertinent literature.

Case reports

Twenty-eight cases of intracranial tumors presenting within the 1st year of life were admitted to the Division of Neurosurgery of Bellaria Hospital, Bologna, over an 18-year period (January 1970 to March 1988). Only clearly symptomatic tumors under the age of 1 year were included in the study. Although 8 patients came under the direct care of the neurosurgeon beyond the 12th month, the earlier onset of symptoms was documented in all cases with absolute certainty. The salient clinical features of the series are summarized in Tables 1 and 2. Six supratentorial tumors (cases 1–6) produced symptoms within the first 2 postnatal weeks, 3 of which already at birth; the other supratentorial cases were more evenly distributed throughout the following months. The infratentorial locations tended to cluster around the end of the year. Males (18 cases) outnumbered females in the series; the supratentorial location (19 patients) was dominant over the infratentorial location (9 cases). The time elapsed from the onset of symptoms to the diagnosis ranged between 1 day (case 14) and 17 months (case 10), the mean interval being similar for supratentorial (3.6 months) and infratentorial (3.1 months) locations. The longest history (17 months) was observed in a girl who developed left sided seizures and ipsilateral progressive hemiparesis at the age of 5 months (case 10). The presumptive diagnosis of cerebral palsy had been put forward by her pediatrician and maintained until 22 months when a neuroradiological assessment revealed a large meningioma of the right frontoparietal convexity. The tumor, of the fibroblastic variety, was totally resected with a definite improvement of the neurological conditions.

A tissue pathological diagnosis was established in 24 cases either by operation or at autopsy. The remaining 4 tumors (cases 1, 3, 5, 25) were diagnosed by neuroradiological work-up; these histologically undetermined neoplasms all were large in size and deep in location, ruling out a conceivable surgical salvage. Three of these

Offprint requests to: E. Galassi

Table 1. Supratentorial tumors. CHT, Chemotherapy; CT, computerized tomography; HY, hydrocephalus; IR, interstitial radiotherapy; PNET, primitive neuroectodermal tumor; RT, radiotherapy; Tork., Torkildsen; VP, ventriculoperitoneal

Case	Sex	Age at onset/ initial presentation	Age at diagnosis (months)	Histology	Location	HY	Symptoms and signs (at diagnosis)	Shunt	Direct operation	Course	RT/ CHT	Outcome follow-up
1	M	Birth/ macrocrania	2	Not verified	III Ventricle	+	Macrocrania, opisthotonos	VP	–	Pulmonary infective complications, 2 months post-op death	–	Dead (2 months)
2	M	Birth/occipital scalp swelling	5	Dermoid	Occipital midline, extra-intracranial	–	Macrocrania, delayed milestones, hypertricotic occipital scalp swelling	–	Total	Uneventful	–	Alive (15 years), mild retardation
3	M	Birth/ macrocrania	2	Not verified	Pineal-III ventricle	+	Macrocrania, VI nerve palsy	Tork.	–	Rapid tumor progression	–	Dead (4 months)
4	M	1 day/seizures	2	Ganglioglioma	Right frontal	–	Seizures, lethargy	–	Subtotal	Uneventful	–	Alive, doing well (6 years)
5	M	4 days/ macrocrania	2	Not verified	Right temporal basal ganglia	+	Macrocrania, emaciation, extensor attacks	VP	–	Sudden deterioration with coma and death before direct operation	–	Preoperative mortality
6	F	2 weeks/ seizures	2	Giant cell astrocytoma	Right fronto-parietal	–	Tuberous sclerosis: depigmented ash-leaf macules; seizures	–	Total	Uneventful	–	Alive (2 years), mild retardation
7	M	2 months/ macrocrania	3	Choroid plexus papilloma	Left lateral ventricle (trigone)	+	Macrocrania, delayed milestones	–	Total	Postoperative subdural CSF effusion	–	Alive, doing well (2.5 years)
8	F	2 months/ irritability	4	Choroid plexus papilloma	Left lateral ventricle (trigone)	+	Macrocrania, vomiting, lethargy, emaciation, right hemiparesis, extensor attacks	–	–	Emergency external ventricular drainage, sudden respiratory arrest and death before direct operation	–	Preoperative mortality
9	F	4 months/ macrocrania, vomiting	5	PNET	Right parieto-temporal	+	Macrocrania vomiting seizures	–	Total	Postoperative subdural CSF effusion	CHT	Alive, moderate retardation (1.5 years)
10	F	5 months/left hemiparesis, seizures	22	Meningioma (fibroblastic)	Right fronto-parietal	–	Left hemiparesis, seizures	–	Total	Uneventful	–	Alive (6 years), markedly improved
11	M	6 months/ macrocrania, vomiting	7	Ependymoma	III Ventricle	+	Macrocrania, vomiting, papilledema	–	Partial	Temporary external ventricular drainage	RT	Dead (3 months)
12	F	8 months/ macrocrania poor feeding	9	Choroid plexus papilloma	Right lateral ventricle (trigone)	+	Macrocrania, lethargy, emaciation, delayed milestones	–	–	Increasing lethargy and coma, emergency external ventricular drainage, progressive deterioration and death	–	Preoperative mortality

Table 1 (continued)

Case	Sex	Age at onset/ initial presentation	Age at diagnosis (months)	Histology	Location	HY	Symptoms and signs (at diagnosis)	Shunt	Direct operation	Course	RT/ CHT	Outcome follow-up
13	M	9 months/ macrocrania, development regression	11	Glioblastoma	Frontal bilateral	+	Macrocrania, lethargy, delayed milestones, VI nerve palsy	–	Partial	Sudden respiratory arrest and coma, death 1 day post-op	–	Surgical mortality
14	F	10 months/ seizures	10	PNET	Left temporoal	–	Seizures	–	Subtotal	Refractory brady-cardia and hypo-tension, death 1 day post-op	–	Surgical mortality
15	M	10 months/ macrocrania	12	Choroid plexus papilloma	Left lateral ventricle	+	Macrocrania, lethargy, delayed milestones	–	Total	Postoperative sub-dural CSF effusion	–	Alive, doing well (4 months), mild retardation
16	M	11 months/ macrocrania	16	Choroid plexus papilloma	Right lateral ventricle (trigone temporal horn)	+	Macrocrania, irritability	–	Total	Uneventful	–	Alive (3 years), doing well
17	F	11 months/ vomiting, poor feeding	18	Ependymoma	Right parieto-temporal	+	Vomiting, left hemi-paresis, failure to thrive	VP	Subtotal	Uneventful	RT	Dead (2 years, 4 months)
18	M	Operated for myelomeningo-cele and hydro-cephalus 11 months failure to thrive	18	Cranio-pharyngioma	Supra-retro sellar	+	Emaciation, delayed milestones, optic atrophy, paraparesis	VP	1 Partial 2 Partial	Two direct oper-ations, subdural CSF effusion (burr hole evacuation)	–	Dead (4 months)
19	F	11 month/ right hemi-paresis	20	Benign astro-cytoma	Left thalamus	–	Right hemiparesis	–	Stereo-tactic biopsy	Uneventful	IR	Alive (16 months), markedly improved, noticeable tumor reduction at CT

Table 2. Infratentorial tumors. CHT, Chemotherapy; CT, computerized tomography; HY, hydrocephalus; RT, radiotherapy; VP, ventriculoperitoneal

Case	Sex	Age at onset/ initial presentation	Age at diagnosis (months)	Histology	Location	HY	Symptoms and signs (at diagnosis)	Shunt	Direct operation	Course	RT/ CHT	Outcome follow-up
20	M	2 months/ vomiting, macrocrania	2	Benign astrocytoma	IV Ventricle, brain stem	+	Macrocrania, vomiting	–	Subtotal	Uneventful	RT	Alive, doing well (9 years)
21	F	5 months/ macrocrania	9	Benign astrocytoma	Vermis, left cerebellar hemisphere, IV ventricle	+	Macrocrania, vomiting, delayed milestones	–	1 Partial 2 Subtotal	Reoperation 1 year after 1st intervention (tumor progression)	–	Alive, doing well 1 year and 4 months
22	F	9 months/ vomiting, poor feeding	12	Medullo-blastoma	IV Ventricle, right cerebellar hemisphere	+	Macrocrania, vomiting, lethargy, emaciation, papilledema, extensor attacks	–	–	Increasing lethargy and coma, emergency ventricular drainage respiratory arrest	–	Preoperative mortality
23	M	10 months/ macrocrania, vomiting, irritability	12	Benign astrocytoma	Right cerebellar hemisphere	+	Macrocrania, head tilt, vomiting, irritability, failure to thrive, extensor attacks	–	Total	Uneventful	–	Alive, doinig well (6 years)
24	M	10 months/ macrocrania	17	Benign astrocytoma	Vermis, right cerebellar hemisphere	+	Macrocrania, VI nerve palsy, papilledema, ataxia, delayed mile-stones	–	Total	Post-operative deterioration and coma, death (1 day post-operation)	–	Surgical mortality
25	M	11 months/ irritability, poor feeding, vomiting	12	Not verified	Brain stem (pons)	+	Vomiting, failure to to thrive, VII nerve palsy, head tilt, irritability	–	–	Tumor progression	RT	Dead (1 year)
26	M	11 months/ vomiting, macrocrania, development regression	13	Benign astrocytoma	IV Ventricle, brain stem	+	Macrocrania, head tilt, emaciation, papilledema, extensor attacks, vomit-ing, delayed milestones	–	Subtotal	Post-op pulmonary complication (pneumothorax), death	–	Surgical mortality (4 days post-op)
27	M	11 months/ vomiting	20	Benign astrocytoma	Right cerebellar hemisphere	+	Vomiting, ataxia, head tilt, papilledema	VP	Total	Uneventful	–	Alive, doing well (8 years)
28	M	12 months/ head tilt, poor feeding	12	Ependymo-blastoma	IV Ventricle	+	Head tilt, papilledema, poor feeding	–	Subtotal	Temporary external ventricular drainage, post-op course uneventful	RT	Dead (4 months)

four infants (cases 1, 3, 25) were deliberately submitted only to palliative treatment (shunt operation or radiotherapy); the fourth infant (case 5) irreversibly deteriorated and died after CSF shunting and before the direct surgical exploration. The histological distribution of the 24 verified tumors was as follows: 8 astrocytomas (7 benign astrocytomas and 1 giant cell astrocytoma), 5 choroid plexus papillomas, 3 ependymal tumors (2 ependymomas, 1 ependymoblastoma), 2 primitive neuroectodermal tumors, and one each of a dermoid, craniopharyngioma, ganglioglioma, glioblastoma, medulloblastoma, and meningioma.

Benign astrocytoma dominated below the tentorium (6/9 infratentorial neoplasms), while choroid plexus papilloma (5 cases) was the chief supratentorial type. All choroid plexus tumors were located within one lateral ventricle and had caused marked hydrocephalus (Figs. 2–4). The subependymal giant cell astrocytoma (case 6) presented as a solitary, medium-sized, paraventricular mass in a neonate investigated because of seizures and cutaneous macules suggesting tuberous sclerosis. This tumor was successfully resected after thorough cardiological evaluation failed to demonstrate the existence of associated cardiac rhabdomyomas. The congenital dermoid (case 2) consisted of an extracranial component, already evident at birth, connected with a large intracranial mass expanding interhemispherically within a duplication of the falx cerebri.

The majority of our tumors (15 cases) exhibited intraventricular or paraventricular sites (case 1, 3, 6–8, 11, 12, 15–17, 20–22, 26, 28); hydrocephalus, of varying degree, was associated in 22 cases (78.6%), including all infratentorial locations.

As for the initial clinical picture, increasing head size (15 cases) and vomiting (9 cases) were the most common presenting features. Behavioral changes with irritability and/or poor feeding (food refusal) were also frequently reported at the early stages of the disease (7 cases). At the time of diagnosis macrocrania (18 cases) was the dominant physical finding and vomiting (11 cases) the most frequent symptom. Nine infants showed delayed milestones due either to an arrested or even regressed psychomotor development. Upon admission, 6 patients appeared abnormally lethargic whereas 3 were irritable and hyperalert. Insufficient weight gain with failure to thrive or definitely emaciated conditions were observed in 9 instances. True inanition together with impaired neurological functions had led at least 4 infants to a severe compromise of their general status (cases 5, 8, 12, 22). These 4 patients irreversibly deteriorated and died before any direct attack upon the tumor could be attempted.

Papilledema was found in six instances, and its incidence was highest among the infratentorial locations (5/9 cases). Five infratentorial cases showed head tilt. Opisthotonos and typical extensor attacks occurred in three infratentorial and three supratentorial tumors. Five patients with supratentorial hemispheric localizations had experienced seizures. The incidence of focal signs was low: hemiparesis developed in 4 cases (8, 10, 17, 19), unsteadiness and truncal ataxia were seen in 2 infratentorial cases (24, 27) of children who had already begun to walk.

Optic atrophy was associated with the suprasellar craniopharyngioma; this case (case 18) is particularly noteworthy because of the exceptional combination of meningomyelocele and craniopharyngioma. Soon after birth the infant had received surgical treatment for congenital hydrocephalus and meningomyelocele. He then fared satisfactorily until the 11th month, when failure to thrive and increasingly delayed psychomotor development were noticed. He was readmitted at the age of 18 months with a presumptive diagnosis of shunt malfunction and CT examination revealed the suprasellar tumor. The patient succumbed at the end of the 2nd year of life after two repeat operations which failed to achieve a complete eradication of the craniopharyngioma.

The radiological diagnosis was established in 22 cases by computerized tomography (CT) (Figs. 1–5). Before the introduction of CT scanning (6 cases), angiography and/or air studies (encephalography-ventriculography) were the chief diagnostic tools. Additional cerebral angiography was performed in ten tumors, primarily detected by CT, in order to provide further information on arterial supply and tumor vascularity. Before approaching vascularized choroid plexus papillomas carotid and vertebral angiograms were customarily undertaken, affording identification of the main anterior and posterior choroidal feeders (Figs. 2, 3).

Two patients were examined by MRI (Fig. 5) and two others had been preliminarily evaluated using ultrasound studies.

Treatment and results

Eight infants in the series were not treated with direct surgical attack for tumor removal (cases 1, 3, 5, 8, 12, 19, 22, 25). Four of them (cases 5, 8, 12, 22) were admitted in severely compromised conditions and underwent emergency CSF diversions (three external ventricular drainages and one VP shunt), but rapidly deteriorated and died before any cranial operation could be attempted. Noticeably there were two benign choroid plexus papillomas among them. In the remaining 4 patients (cases 1, 3, 19, 25) the direct approach was considered ill-advised because of relevant size and/or deep location of the tumors. Of these last 4 infants, one (case 1) succumbed to pulmonary complications 2 months after VP shunting and 1 (case 3) died of tumor progression 4 months after a Torkildsen ventriculocisternostomy. Another infant (case 25), affected by a brain-stem pontine tumor and treated by conventional radiotherapy, died 1 year post diagnosis.

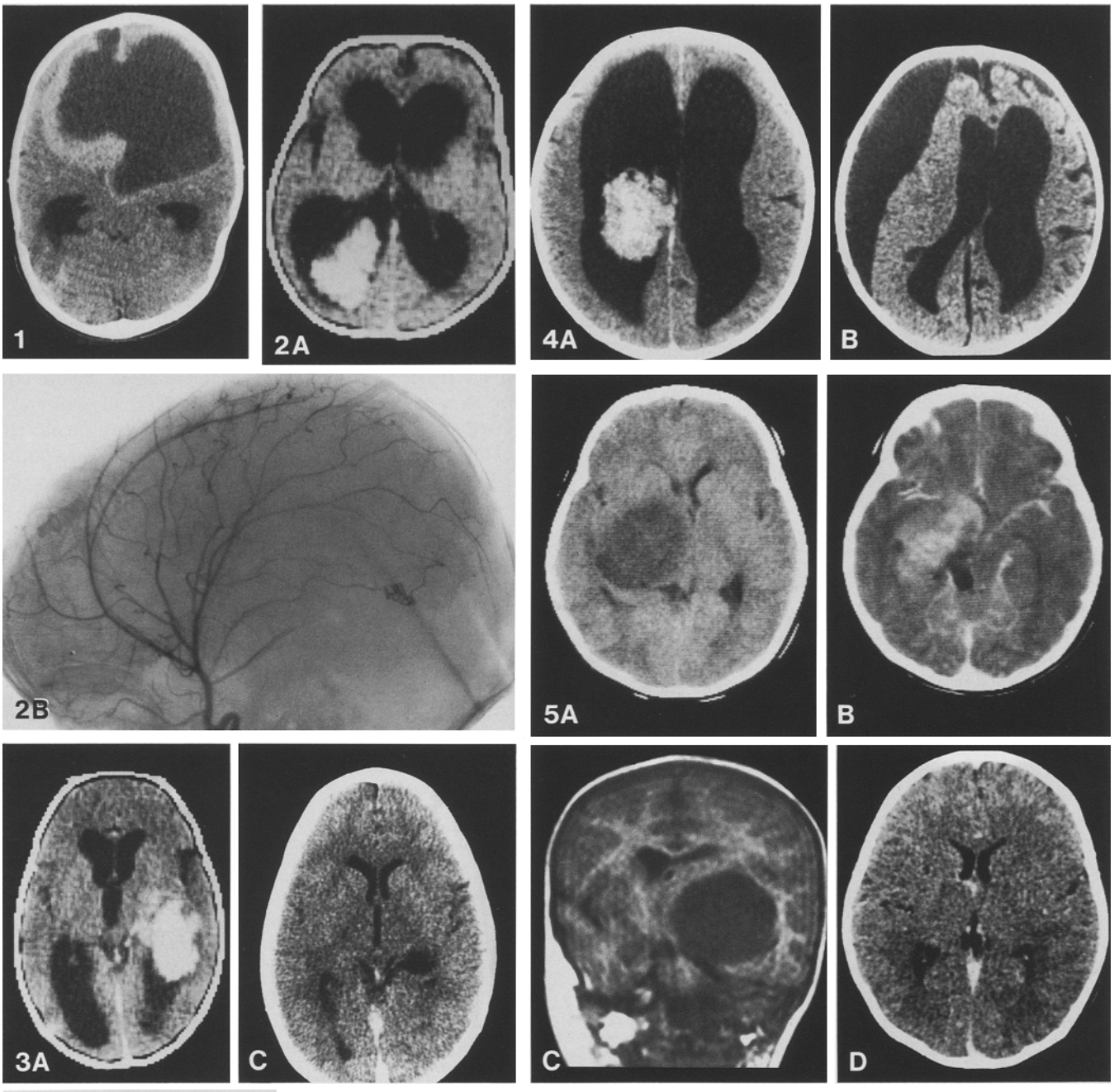
The only surviving patient who was not submitted to direct tumor resection had a large thalamic benign astrocytoma (case 19): stereotactic biopsy and interstitial implantation of two I^{125} seeds were accomplished resulting in definite neurological improvement and steady reduction of the tumor bulk at follow-up CT control (Fig. 5).

Direct approaches were performed in 20 patients. A radical resection of the neoplasm was achieved in 10 cases; subtotal or partial removals were accomplished in 7 and 3 patients respectively. Repeat surgery was performed in two cases (cases 18, 21) where the neoplasm had been only partially excised. Four of the 20 operated cases died within 1 month (cases 13, 14, 24, 26), for a surgical mortality of 20% in the series.

Subdural CSF effusion represented a rather common post-operative complication in the supratentorial tumors, occurring in two choroid plexus papillomas (Fig. 4), one large primitive neuroectodermal tumor (case 9), and in the suprasellar craniopharyngioma (case 18). In three instances, the subdural fluid collection was mainly an expression of the craniocerebral disproportion secondary to removal of large tumors and severe hydrocephalus; in one case (case 18) it was progressive and symptomatic and required burr hole evacuation.

After tumor removal, progression of associated hydrocephalus occurred in 2 of the survivors (cases 17, 27), requiring VP shunt insertion. External focal radiation therapy was administered to 4 patients (cases 11, 17, 20, 25); spinal and whole brain irradiation was given only to 1 infant (case 28) harboring an ependymoblastoma of the IV ventricle.

Eight infants suffered preoperative or surgical mortalities. In the remaining 20 cases the follow-up period ranged



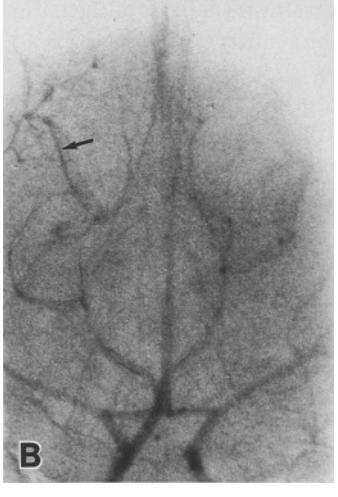


Fig. 1. Case 13, glioblastoma. Contrast-enhanced computed tomography scan shows a huge cystic tumor invading both frontal lobes. Ventricular dilation is associated

Fig. 2A, B. Case 7, choroid plexus papilloma. **A** Contrast-enhanced computerized tomography shows a markedly enhanced mass in the trigone of the left lateral ventricle. Generalized hydrocephalus is associated. **B** Carotid angiogram demonstrates tumor vascularity supplied by the anterior choroidal artery

Fig. 3A–C. Case 16, choroid plexus papilloma. **A** CT scan after contrast injection shows a large enhancing mass in the trigone and temporal horn of the right lateral ventricle. There is marked hydrocephalus. **B** Vertebral angiogram reveals neovascular strain supplied by an enlarged right posterior choroidal artery (*arrow*). **C** Postoperative CT scan (2 years after surgery): tumor excision has resulted in a definite regression of hydrocephalus

Fig. 4A, B. Case 15, choroid plexus papilloma. **A** Preoperative CT scan shows a contrast-enhancing tumor in the left ventricle with attendant hydrocephalus. **B** Subdural CSF effusion and marked cerebral collapse following tumor removal are observed at postoperative CT control

Fig. 5A–D. Case 19, benign astrocytoma. **A, B** Pre- and postcontrast CT scans and **C** magnetic resonance imaging disclose a large roundish left thalamic neoplasm with considerable mass effect. **D** CT scan 1 year after stereotactic biopsy and implantation of two I125 seeds show an impressive reduction in size of the tumor mass and complete regression of the ventricular displacement

from a few months to 15 years (case 2): 13 of these patients are currently alive.

The majority of deaths during the follow-up period (6/7) occurred within the first 12 months, in patients with nonoperated or incompletely resected tumors. These deaths, together with the preoperative and surgical mortalities, heavily contribute to the sudden drop in the 1-year survival rate (14/28 cases). One patient affected by a supratentorial ependymoma succumbed 2 years, 4 months post diagnosis.

In 1 of the 13 currently surviving patients (case 15), the length of the follow-up period is rather short (1 year). However, 6 of the 13 survivors were alive 6 to 15 years after diagnosis (cases 2, 4, 10, 20, 23, 27). Of the 12 survivors with more than 1 year follow-up, 7 lead normal lives and 5, although improved, show mild to moderate retardation and/or neurological deficits.

Discussion

Tumors of the CNS are the second most frequent malignancy occurring in infants [13, 22, 25]. According to autopsy studies, they account for 0.04% up to 0.18% of the total deaths under age 1 year [20, 54].

It is generally agreed that a significant, although undetermined, percentage of intracranial tumors presenting in the 1st year developed during intrauterine life. The prenatal origin is obvious in all neoplasms detected in stillborn fetuses [16, 48, 51, 53] as well as in the cases already symptomatic at birth, most of them showing an evident head enlargement [16, 18–20, 33, 48, 50–52]. Not surprisingly, a cephalopelvic disproportion interfering with normal delivery and perinatal troubles are commonly reported in these newborns [16, 18, 20, 41, 51, 55].

As for the tumors presenting some time after birth, the absence of reliable criteria to estimate their postnatal growth makes the definition of indisputably congenital neoplasms rather difficult [38, 49]. Adopting solely chronologic criteria, Solitare and Krigman [45], followed by Wakai et al. [51], restricted the definition of "definitely congenital" to tumors present or producing symptoms at birth, of "probably congenital" to those present or producing symptoms within the 1st postnatal week, and of "possible congenital" to those present or symptomatic within the 1st postnatal months. Nevertheless, the paucity and nonspecificity of neurological manifestations in the early neonatal stages and the extraordinarily huge sizes often observed at the time of diagnosis reasonably suggest that a larger proportion of infantile brain neoplasms are congenital in origin.

Jellinger and Sunder-Plassmann [20] modified Solitare's classification and extended the term of "definitely connatal" to cases presenting within the first 2 weeks, of "probably connatal" to those present or recognized during the 1st year of life, and of "possibly connatal" to those detected beyond 1 year but whose initial symptoms could be traced back to the first 12 months of life.

The supratentorial/infratentorial ratio of intracranial tumors in the 1st year of life differs strikingly from that seen later in childhood. One century ago, Starr [46] stressed the peculiar incidence of cerebellar neoplasms in childhood. Since then, infratentorial tumors have repeatedly been recognized to occur more frequently than the supratentorial ones in children [14, 23, 31]. As a matter of fact, infratentorial locations account for 54.7% of the cases in a recent survey of 1,350 brain tumors from three major children's institutions in North America [5]. However, the topographic distribution during the 1st postnatal year is at a strong variance with such overall data and similar to the adult pattern. In fact, by reviewing 398 tumors of the 1st year of life taken from ten published series [1, 7, 8, 12, 22, 28, 42, 43, 49, 55] and from our material, we found a marked prevalence of supratentorial tumors (255 cases corresponding to 64.1%; Table 3). The proportion is even higher when moving back to the neonatal period [1, 12, 22, 48, 51]. Indeed, Wakai and associates [51] reviewed 200 neonatal brain tumors diagnosed up to the age of 2 months and reported a 73.5% incidence of supratentorial tumors, similar to the figure observed by Jooma et al. [22] and by Takaku et al. [48] for the same age group. No definite sex predilection is deducible for brain tumors below 1 year; the analysis of 279 cases from the literature [8, 12, 22, 28, 38, 42, 44, 55] and from our material reveals an equal incidence (M:F = 141:138, i.e., 50.5% and 49.5%; Table 3).

Table 3. Location and sex incidence of intracranial tumors during the 1st year of life

Sex incidence (279 reviewed cases[a])	Males 141 (50.5%)	Females 138 (49.5%)
Location (398 reviewed cases[b])	Supratentoral 255 (64%)	Infratentorial 143 (36%)

[a] See [8, 12, 22, 28, 38, 42, 44, 55] and present series
[b] See [1, 7, 8, 12, 22, 28, 42, 43, 49, 55] and present series. Even though [1] and [49] deal also with older children, only cases less than 1 year of age are included in the present table

The vast majority of intracranial tumors in infants are neuroectodermal in origin. Table 4 summarizes a review of 343 such histologically verified tumors collected from 11 series, including our own [7, 8, 12, 20, 22, 28, 42, 44, 49, 55]. The neuroectodermal types account for 80.2% of the entire material, with astrocytoma ranking first (108 cases, 31.5%), followed by medulloblastoma (52 cases, 15.2%), choroid plexus papilloma (44 cases, 12.8%), and ependymoma (35 cases, 10.2%). The incidence of teratomas significantly increases when only newborns (2 months) are taken into consideration: these tumors are the most frequent in the neonatal series reported by Wakai et al. [51], and by Takaku et al. [48] accounting for 36.5% and 51.4%, respectively, of all cases. The noticeable representation of choroid plexus tumors (12.8% of the reviewed cases under 1 year; Table 4) is strikingly higher than that reported in the general (0.6%) and even in the solely pediatric (2%–5%) neurosurgical practice [27]. The peculiar predilection of this histological type for the lateral ventricles and early infancy has already been stressed [22, 27, 30, 31, 37, 49, 50]. Laurence estimated

Table 4. Diagnosis in 343 histologically verified intracranial tumors of the 1st year of life[a]

Histological diagnosis		
"Astrocytoma"	60	Total no. of astrocytomas = 108 (31.5%)
Benign (pilocytic) astrocytoma – spongioblastoma	31	
"Superficial astrocytoma attached to dura"	6	
Giant cell astrocytoma (tuberous sclerosis)	3	
Fibrillary astrocytoma	2	
Malignant (anaplastic) astrocytoma	6	
Glioblastoma	8	Total no. of neuroectodermal neoplasms = 277 (80.8%)
Oligodendroglioma	2	
Ganglioglioma	2	
Medulloblastoma	52	
Medulloepithelioma	2	
Retinoblastoma	2	
Neuroblastoma	1	
Ependymoma – ependymoblastoma	35	
Choroid plexus papilloma – carcinoma	44	
PNET	15	
"Primitive glial" tumor	2	
Unclassified glioma	4	
Teratoma	11	
Malignant germ cell tumors	3	
Pinealoma – pineoblastoma	2	
Dermoid	4	
Craniopharyngioma	10	
Hemangioblastoma	5	
Sarcoma	12	
Meningioma	2	
Others	17	

[a] See [7, 8, 12, 20, 22, 28, 42, 44, 49, 55] and present series. Even though [49] deals also with older children, only cases less than 1 year of age are included in the present table

that in 50% of lateral ventricular choroid plexus papillomas the first symptoms appear before the age of 6 months [27]. Many reports also observe that a number of such tumors, with the attendant hydrocephalus, are certainly present at birth [22, 27, 30, 50, 51, 55].

Meningiomas occurring within the 1st year of life are extremely uncommon. Only scattered examples, like the case in our series, have been reported to date. Mendiratta et al. [32], in a review of 2,620 childhood intracranial neoplasms, found 38 (1.5%) meningiomas, only two of which were in infants; Herz and coworkers [17] brought together 112 previously published pediatric meningiomas and summarized the features of the 6 cases aged up to 12 months. An analysis of the available literature [3, 6, 7, 9, 10, 23, 26, 29, 32, 35, 36, 40, 45, 53] indicates that about 35 intracranial meningiomas presenting under the age of 1 year have been published, the majority of which are of the fibroblastic or angioblastic varieties. This tumor type, as well, can sometimes develop prenatally, as is substantiated by the large sizes frequently seen at diagnosis and by the exceptional findings in a stillborn fetus and in neonates [9, 10, 29, 36, 45, 53].

The newborn with tuberous sclerosis and associated giant cell astrocytoma (case 6) also seems noteworthy in the present series: after the two cases described by Painter et al. [33] this would be the third symptomatic neonatal giant cell astrocytoma documented in the literature and the first successfully treated by surgical removal.

In their series of connatal brain tumors, Jellinger and Sunder-Plassmann [20] previously cited one other case of tuberous sclerosis which, however, was diagnosed after 1 year of age. Tomita and McLone [49] have listed such an histological type in their 57 tumors occurring within the first 12 months, but detailed clinical information is lacking about the patient. Although CNS neoplasms related to tuberous sclerosis are usually recognized later in childhood, the average age at presentation being 13.5 years according to Boesel et al. [4], the above observations suggest that they can develop earlier, antenatally or neonatally.

The large size of the tumor mass, especially if supratentorial (Fig. 1), and the high incidence of associated hydrocephalus are of paramount importance in intracranial tumors during the 1st year of life [4, 8, 12, 21, 28, 38, 55]. The readily expansile skull, widened extracellular and subarachnoid spaces, and plastic and adaptive capacities of the poorly myelinated undeveloped brain delay the onset of symptomatic intracranial hypertension and allow considerable tumor growth in contrast with a surprising scarcity of focal deficits [1, 13, 21, 28, 38, 49, 55]. Associated hydrocephalus was observed in the 78.6% of our case material and even higher figures ranging from 80% to 92% are reported in other series [21, 49, 55].

This prominent association conceivably depends on the high number of intra- and paraventricular forms [42], midline locations [22, 42, 49], and magnitude of the neoplasm encroaching upon and severely distorting the ventricular system. Distal subarachnoid block as a result of repeat tumor bleedings along with CSF oversecretion are the most likely factors causing hydrocephalus in the case of choroid plexus papillomas [27, 30].

The clinical picture of infantile intracranial tumors tends to be subtle and nonspecific in the early stages of the history: the diagnosis is hampered by the lack of verbal complaints and ambulation, the often defective parental information, and the paucity of localizing manifestations. Not uncommonly, and particularly before the availability of noninvasive imaging techniques, these infants have been referred to neurosurgical consultation after incorrect tentative diagnoses of meningitis, intracranial hemorrhage, cerebral palsy, gastroenteritis, subdural effusion, or conventional hydrocephalus [1, 8, 20, 21, 22, 24, 44, 48, 55]. The delay in diagnosis is sometimes responsible for serious deterioration of the general and nutritional status: persistent lethargy, vomiting and feeding difficulties may, in fact, easily lead these infants to dehydration, anemia, and severe emaciation. Vomiting is the most common symptom with a reported incidence between 39.2% and 56% in the larger series [1, 22, 49, 55]. The frequency of a behavioral syndrome characterized by irritability, hyperalertness, or, conversely, poor responsiveness and lethargy is also significant [1, 8, 21, 22, 38, 49, 55, present series]. Some authors [8, 13, 22] have also called attention to the value of an arrest or regression of the

psychomotor development as a frequent and sensitive indicator of CNS disturbance in these infants. Increased head circumference, reflecting the adaptive capacities of the infantile skull to an enlarging intracranial content, is by far the dominant physical finding; macrocrania was observed in 64% of the patients of Jooma et al. [22] and in our material; but, much higher figures, 83% and 82% respectively, were reported in the series by Sano [43] and by Sakamoto et al. [42]. The expansibility of the skull affords a compensating mechanism to raising intracranial pressure; this accounts for the comparatively low occurrence of papilledema (mostly below 30%) despite frequently huge tumor bulks [8, 12, 13, 38, 43, 49, 55, present series]. Similarly, due to the deformability of the poorly myelinated brain, focal or lateralizing manifestations such as seizures or hemiparesis develop uncommonly, being present in 10%–20% of the patients [1, 12, 13, 22, 28, 49, 55, present series]. It is worth noticing that alarming or definitely critical signs including stiffness and abnormal posture of the neck [13, 22, 28, 38, 49], opisthotonos and typical cerebellar attacks [22, 32, 34, 51, 55], respiratory disturbances [20, 42, 48, 51], and coma [13, 38, 39, 48, 49] were occasionally detected at the first neurosurgical evaluation. It is apparent that such initially deteriorated neurological conditions, besides attesting to a frequently delayed diagnosis, heavily contribute to many dismal and even fatal courses. This is confirmed by a number of early preoperative deaths recorded in the literature [20, 22, 43, 55, present series].

Although uncommonly documented, spontaneous intratumoral hemorrhage is one of the conceivable sources of sudden clinical deterioration; according to Wakai et al. connatal brain neoplasms would exhibit a particular tendency to bleed during the neonatal period [36, 39, 51].

Management and conclusions

Three kinds of problems are fundamentally encountered in the management of infantile intracranial tumors:

1. Indication and timing of CSF shunting

2. Feasibility and technical difficulties related to the direct tumor approach

3. Advantages and adverse effects of adjunctive radiochemotherapy

As for the first issue, Raimondi and Tomita [38] stressed the value of preliminary shunting, especially if the infant is critically ill from severe intracranial hypertension and/or seriously impaired general conditions. The procedure is credited to be beneficial, relieving raised intracranial pressure and allowing time for physical and nutritional improvement; furthermore, it can favor cerebral reexpansion, thus lowering the risk of intra- or postoperative brain collapse [28, 38, 42]. Twenty-eight of the 32 hydrocephalic cases were shunted prior to craniotomy in Raimondi's series, all experiencing significant clinical improvement [38]. However, CSF diversions, though simple, entail inherent complications in tumors: acute abdominal distension due to oversecreting choroid plexus papillomas [38, 49] and peritoneal pseudocysts secondary to high CSF protein content in cases of chiasmatic gliomas [55] and teratomas [18] have been occasionally observed in infants.

Such abdominal complications occurred in 4 of the 28 patients preliminary shunted by Raimondi and Tomita [38] and in 2 of the 15 infants who received the ventriculoperitoneal diversion in the study of Zuccaro et al. [55].

Upward transtentorial herniation with coma, as reported by Tomita and McLone in one infantile case [49] is a well-known potential complication of ventricular shunting in patients harboring infratentorial masses. Postoperative deaths after simple shunt operation have been recorded in some infantile tumor series [8, 12, 22, 55, our case 1]. Jooma et al. reported two operative deaths among 14 ventricular shunting procedures [22].

Zuccaro and associates [55] have advocated primary tumor removal as an effective and possibly definitive treatment of abnormal CSF dynamics: 14 of their 33 hydrocephalic infants submitted to direct tumor resection exhibited postoperative remission of hydrocephalus, thus making a subsequent shunt insertion unnecessary. Only 2 out of our 11 hydrocephalic patients surviving after direct operations required VP shunting, whereas tumor removal per se enabled a permanent relief of hydrocephalus in the other 9 cases (Fig. 3). Laurence [27] considers temporization with preliminary shunting to be ill-advised, and recommends prompt tumor removal when faced with choroid plexus papillomas; the same author postulates a presumed peculiar vulnerability of such patients in whom acute worsening might be precipitated by a simple ventricular tapping. Actually, two of our five cases of choroid plexus papillomas (cases 8–12) fatally continued to deteriorate after external ventricular drainage; the remaining three infants did well after their lateral ventricular papillomas were resected and did not require any postoperative CSF diversion. This latter behavior is in accordance with Matson's experience in which hydrocephalus appeared constantly relieved after successful removal of lateral ventricular choroid plexus papillomas [30], but noticeably in contrast with Raimondi's results in which persisting hydrocephalus required CSF shunting in the great majority of the operated choroid plexus tumors [37].

Directly approaching an intracranial tumor during the 1st year of life represents a challenging task, entailing complex anesthesiological and surgical problems. The intrinsic difficulties are reflected by some high surgical mortality rates gleaned from the literature [8, 21, 22, 42, 43] even though the recent advances in neurosurgical techniques and pediatric supportive anesthesiological management have invaluably contributed to the decline in the operative mortality [1, 22, 28, 49, 50].

From the anesthesiological viewpoint, there has been growing concern about the importance of accurately estimating blood losses and scrupulous monitoring of the body temperature, fluid and electrolyte balance, and respiratory and cardiovascular parameters [1, 22]. The peculiar sensitiv-

ity of newborns and infants to intraoperative bleeding and hypothermia exposes them to the danger of severe hypotension, bradycardia, and cardiac arrhythmias [1, 13, 22, 30, 49]. Unfortunately, many infantile neoplasms, and above all choroid plexus papillomas, are exceedingly large and vascular and major sudden hemorrhages may ensue during tumor manipulation; in such circumstances the small blood volume of the infant calls for a prompt replacement with fresh blood to prevent irreversible shock and intraoperative catastrophes [1, 30, 37, 50]. Raimondi and Gutierrez [37], and Tomita and Naidich [50] have emphasized the critical importance of detailed preliminary angiographic evaluation of the tumor vascularity and arterial feeders when dealing with choroid plexus neoplasms in order to facilitate the surgical control of the main vascular pedicles and prevent risky intraoperative hemorrhages.

Newborns with tuberous sclerosis and subependymal giant cell astrocytomas raise special problems as refractory, life-threatening arrhythmias may develop intraoperatively, possibly related to associated cardiac rhabdomyomas [1, 33]. Extensive cardiological work-up has, therefore, been recommended in such cases by Painter et al. [33]; the same authors advise a conservative attitude and delayed operation, beyond the neonatal period, if such cardiac neoplasms are detected.

From the strictly technical standpoint, the fundamental difficulties arise from huge tumor sizes, deep-seated locations, hypervascularity, and from the sometimes enormous dilation of the ventricular system.

Considerable care is needed in operating on tumors in the severely hydrocephalic infant: cerebral collapse due to ventricular CSF escape and bleeding from avulsed cortical veins are conceivable complications when dilated ventricles are entered approaching intra- or paraventricular lesions [1, 30, 50]. Scrupulous refilling of the ventricular system is mandatory in order to avoid such a contingency during operation, and, particularly, after the completion of tumor removal. Despite this precaution CSF outpouring and ventricular collapse are not infrequent postoperatively and may easily lead to subdural fluid effusions (Fig. 4); these, in turn, are also facilitated by the steady decrease in the hemispheric volume secondary to the removal of huge tumor bulks [42, 50, present series].

The final controversial issue pertains to the usefulness and contraindications of adjunctive ratio- and chemotherapy. Radiation therapy (RT) can reasonably increase the median survival time for infants harboring malignant and unresectable brain neoplasms [22]. On the other hand, there has been growing awareness, as evidenced in the recent literature, about the deleterious effects of ionizing radiations upon the developing CNS during the early stages of life [1, 11, 22, 26, 38].

Even though the contribution of the tumor mass, hydrocephalus, and intracranial hypertension to the future neurological morbidity of these infants should not be underestimated, intellectual, endocrine, and auxological deficits result from radiating regimens at this age and particularly from whole brain and spinal RT. At the present time, reduced doses and focal fields are generally preferred while caution has been expressed about indiscriminate prophylactic radiotherapy. Conversely, attention has been drawn to the critical importance of radical tumor resection [26, 28, 38, 49, 55], as enabled by modern operative techniques, and to the complementary role of adjunctive chemotherapeutic protocols [1, 26, 28, 43, 49, 55]. Radiating treatment should be reserved for recurrent or metastasizing malignancies and, possibly, for progression of low-grade inoperable tumors such as deeply seated inaccessible astrocytomas. However, as illustrated by one of our cases (Fig. 5), stereotactic interstitial radiotherapy may provide a feasible and effective alternative in the management of these slowly growing, radioresistant tumors [15].

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