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ORIGINAL ARTICLE - PEDIATRIC NEUROSURGERY

Adult outcome after neurosurgical treatment of brain tumours in the first year of life: long-term follow-up of a single consecutive institutional series of 34 patients

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Abstract

Background Long-term results for adult patients who underwent surgery for paediatric brain tumours in the first year of life have not been reported.

Methods We performed a retrospective study on surgical morbidity, mortality rate, academic achievement and/or work participation in patients who underwent primary tumour resection for a brain tumour as infants in the period from 1973 to 1998. Gross motor function and activities of daily life were scored according to the Barthel Index.

Findings Thirty-four consecutive children were included. No patient was lost to follow-up. Twenty-two children (65%) underwent gross total resection (GTR), 10 had subtotal resections (STR) and 2 had only partial resection during primary surgery. Nine children were additionally surgically treated for hydrocephalus (HC), many of them with repeat operations for shunt malfunction during follow-up. Three children died within 30 days following GTR of highly vascular tumours. Seventeen (50%) of the infants had high-grade tumours with 1-month, 1-year and 20-year survival figures of 88, 30 and 30%. The corresponding figures for 17 patients treated for low-grade tumours were 94%, 88% and 88%, respectively. Seventeen patients (50%) are still alive as adult long-term survivors at median age of 29 years (range 20 to 43 years). Three died after 29, 30 and 41 years, respectively. At the latest follow-up, 16 out of 17 long-term survivors have a Barthel Index (BI) of 100, while the remaining one has a BI of 40. Two long-term survivors of a high-grade tumour treated 30 and 35 years ago are severely handicapped and have no working capacity. The 15 long-term survivors after treatment for a low-grade tumour are all in daily activity as students (4), in part-time work (3) or full-time work (8).

Conclusion A brain tumour occurring in the first year of life is a serious threat to the patient and the family, particularly in case of high-grade tumours. In our small cohort, the results from long-term survivors of high-grade tumour group are depressing and confirm the deleterious effect of radiotherapy given to infants decades ago. The infants with low-grade tumours who could be treated with surgical resection without any adjuvant therapy show a good clinical outcome as adults. For parents of these latter patients, the results are far better than feared in advance.

Keywords Infantile brain tumours · Long-term results · Paediatric neurosurgery

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Introduction

Brain tumours occurring in the first year of life are considered to be a disastrous event for the child and its family [1, 3, 11]. The high-grade tumours in infants are often very aggressive, and we could never see small children with posterior fossa medulloblastoma grow up, until the introduction of postoperative radiotherapy at our institution as from 1974, after which half of the children with this tumour survived for 20 years [10]. The deleterious effect of postoperative radiotherapy was recognized during the late 1980s, and treatment without

upfront radiotherapy became standard for children below 3 years of age. Major neurosurgical tumour resections represent also a threat to infants with brain tumours, as well as the tumour disease itself. In addition, many of these children also require surgical treatment for secondary hydrocephalus (HC), and also, adjuvant oncological treatment can be harmful in this age group and lead to permanent damage. Although deleterious effects of different treatment strategies have been debated for several decades, the results have mostly been discussed in terms of survival rates, and long-term clinical results for infants treated for brain tumours have not been extensively reported. We have therefore analyzed the long-term results from treatment of these particular patients, i.e. who were treated for brain tumour as infants for more than 20 years ago, with completed follow-up until adult life.

Method

We retrospectively analyzed a non-selected, consecutive cohort consisting of patients who underwent primary resection of a brain tumour as infants younger than 1 year during the period from 1973 to 1998 at the Department of Neurosurgery, Oslo University Hospital, Oslo, Norway. We define long-term survivors as all patients who have at least a 20-year follow-up and describe their clinical situation at the end of 2018. The cases were identified and collected based on surgical protocols from the study period. The case record data included sex, age at the time of primary tumour resection and data on repeat operations and management of hydrocephalus. To assess the dependence of assistance in daily living, the Barthel Index (BI) score was used [8]. This is a well-established and validated scale using ten variables to measure performance in basic activities of daily living (ADL) primarily related to personal care and mobility. Scores range from 0 to 100; a higher score denotes greater independence. The purpose was to assess functional status and illustrate eventual differences among the patients within the cohort. Educational outcome was simplified and categorized into normal versus special schooling, and employment attendance into open, sheltered or no work.

Results

Clinical results

We identified 34 patients, 18 boys and 16 girls (ratio 1,1), median age 181 (range 3–364) days (Table 1). This series include all cases of primary brain tumour resection in infants younger than 1 year performed at our department in the study period and represent 4.4% of all pediatric tumours of central nervous system operated in the same period of time. The histological examination was performed by an experienced neuropathologist and revealed a high-grade tumour (WHO grade III or IV) in 17 patients; PNET/medulloblastoma in 9, high-grade astrocytoma in 4, anaplastic ependymoma in 2, plexus carcinoma in 1 and 1 high-grade teratoma in 1 patient, respectively. The remaining 17 patients had low-grade tumours: plexus papilloma in 8 (WHO grade I in 5 and grade II in 3 patients), astrocytoma in 5, low-grade gliomas (ganglioglioma, polymorph xanthoastrocytoma) in 2, craniopharyngioma in 1 and low-grade teratoma in 1 patient.

The tumour was localized in the supratentorial compartment in 19 (55%) and in the posterior fossa in 15 infants (45%). Signs and symptoms of increased intracranial pressure (vomiting, rapid head growth, sunset sign) was the leading clinical presentation. Only one child presented with seizures (patient no. 8, Table 1), and in another infant, the clinical presentation was different: a girl with microcrania and failure to thrive; she underwent a STR for a non-cystic craniopharyngioma and never responded favourably to treatment (patient no. 31).

The aim of surgery in these infants was gross total resection (GTR) when feasible which was achieved in 22 patients (Table 1). Three infants died in the early postoperative period after GTR of highly vascular tumours in 1973, 1975 and 1997, respectively. The resection was described by the surgeon as subtotal (STR) in 10 cases. The remaining two patients underwent a partial resection described by the surgeon or according to postoperative imaging. Three patients required repeated resections. This was the case in a child with choroid plexus carcinoma and demonstrated residual tumour on postoperative MRI (patient no. 20) which was resected 2 months after primary resection in 1988. In another patient (no. 19), repeated resection of recurrent posterior fossa ependymoma was undertaken 1 year following primary surgery.

Patient no. 25 (Table 1) presenting with tetraplegia and respiratory arrest had repeated but only partial resections of a lipoma in medulla oblongata after 8 and 10 years, and this patient underwent her first shunt implantation after 28 years. In total, nine children received shunts due to secondary hydrocephalus, many of them requiring shunt revision during follow-up.

Thirteen out of 19 (68.4%) infants with supratentorial tumours are alive at latest follow-up, and the observed 20-year survival is 14/19 (73%). Only 2 out of 15 (13.3%) infants with posterior fossa tumours are alive, yet the observed 20-year survival rate was 4/15 (26%). In total, out of all the 34 children operated for more than 20 years ago, 17 (50%) are still alive, and the observed 20-year survival is 20/34 (58%).

Fifteen out of 17 infants (88%) with low-grade tumour are alive after a 20–43-year follow-up (median 29 years).

Table 1 Clinical results

Pa.nr	Year	Age	Localizat	Histol	Resection	Adjuvterap	Age at LF	Outcome BI	Work?
1	1973	F 161	Supra	GBM	GTR	No	P.o.D	Dead	
2	1975	M 359	Supra	CPP	GTR	No	P.o.D	Dead	
3	1975	F 98	PF	Astro	GTR	No	43 years	100	FTW
4	1975	F 227	PF	PNET	GTR	RT	41 years	Dead	
5	1978	M 279	PF	PNET	GTR	RT	30 years	Dead	
6	1979	M 170	PF	PNET	GTR	RT	4 years	Dead	
7	1980	M 296	Supra	Astro	STR	No	38 years	100	FTW
8	1980	F 271	Supra	DIG	GTR	No	38 years	100	PTW
9	1981	M 254	Supra	CPP	GTR	No	37 years	100	PTW
10	1982	F 310	Supra	CPP	GTR	No	37 years	100	FTW
11	1982	F 171	Supra	GBM	GTR	RT	29 years	Dead	
12	1983	F 364	PF	Epen	GTR	RT	35 years	100	No
13	1984	F 237	Supra	GBM	STR	RT?	5 months	Dead	
14	1984	M 192	PF	PNET	STR	RT	1 months	Dead	
15	1986	F 270	PF	AsHG	STR	No	7 months	Dead	
16	1987	F 164	Supra	PNET	GTR	RT, CT	9 months	Dead	
17	1987	F 110	PF	Terat	ParR	No	3 months	Dead	
18	1987	M 177	Supra	CPP	GTR	No	31 years	100	FTW
19	1988	M 334	PF	Epen	STR	RS	31 months	Dead	
20	1988	M 66	Supra	CPC	STR	RS	30 years	100	No
21	1989	M 313	PF	PNET	STR	RT, CT	9 months	Dead	
22	1989	M 181	Supra	As-II	GTR	No	29 years	100	Stud
23	1990	M 45	Supra	Astro	GTR	No	28 years	100	FTW
24	1990	F 124	PF	PNET	STR	No	2 months	Dead	
25	1990	F 46	PF	Terat	ParR	RSx2	28 years	40	Stud
26	1990	M 3	PF	Astro	GTR	No	28 years	100	FTW
27	1991	M 18	Supra	CPP	GTR	No	27 years	100	FTW
28	1995	M 187	Supra	PXA	GTR	No	23 years	100	PTW
29	1995	F 298	Supra	CPP	GTR	No	23 years	100	Stud
30	1996	M 245	PF	PNET	STR	CT	11 months	Dead	
31	1996	F 337	Supra	Cran	STR	No	3 months	Dead	
32	1997	F 4	PF	PNET	GTR	No	1 day	Dead	
33	1997	M 148	Supra	CPP	GTR	No	21 year	100	Stud
34	1998	M 147	Supra	CPP II	GTR	No	20 year	100	FTW

Sex (F/M), age in days

PXA, pleomorphic xanthoastrocytoma; *Supra*, supratentorial *Cran*, craniopharyngioma; *PF*, posterior fossa; *Terat*, teratoma; *GBM*, glioblastoma; *RT*, radiotherapy; *CPP*, choroid plexus papilloma; *CT*, chemotherapy; *CPC*, choroid plexus carcinoma; *LF*, latest follow-up; *Astro*, astrocytoma; *BI*, Barthel Index; *AsHG*, high-grade astrocytoma (III); *FTW*, full-time work; *DIG*, diffuse infantile ganglioglioma; *PTW*, part-time work; *Epend*, ependymoma (anaplastic); *Stud*, student; *PNET*, primitive neuroectodermal tumour; *RS*, repeat surgery

Adjuvant therapy

Only infants with high-grade tumours in this series received adjuvant therapy. Out of 17 patients, 7 were given postoperative radiotherapy, according to protocol at the given point of time. Some of these infants also received chemotherapy (Table 1). During the last 10 years of the study period, upfront radiotherapy was abandoned in this age group. In some of these infants, adjuvant therapy could not be administered, either due to advanced disease or complications.

Activities of daily life

All except one long-term-survivor have a good gross motor function. Their management of the activities of daily life is

good. Barthel Index score is 100 in all these patients, except for one patient (no. 25, Table 1) who has a BI of 40.

School, education and work

Only five children in the high-grade tumour group reached school age. All these needed assistance, and special schooling; three of them could perform simple practical sheltered work as teenagers.

All the 15 children in the low-grade group followed a normal school program, though with some assistance in four patients. They all finished school, and 4 of them are still students, 3 are in part- or full-time sheltered work, and the majority (8 adults) are in normal full-time employment.

Discussion

This report present complete follow-up data sets of all infants under 1 year of age who underwent operative treatment for brain tumour during a period of 25 years at our institution. As the prognosis for these patients has traditionally been considered dismal, particularly in case of high-grade tumours, we have chosen this study period not only to achieve survival figures but also to highlight data on educational outcome and working ability among the adult long-term survivors. In our small cohort of 34 individuals, 17 were treated for highly malignant tumours according to protocols that during the first 15 years of the study period, also, postoperative radiotherapy was included when feasible. One-month and 1-year survival figures from this group were 88% (15/17) and 41% (7/17), respectively. We were particularly impressed to see that the 5-year survival rate was close to 30% (5/17).

All these 5 individuals were treated more than 30 years ago and were still alive after 20 years. The dark side of this story is that three of them died at the age of 29, 30, and 41 years, most probably due to late effects from radiotherapy. The other two long-term survivors in this subgroup are aged 30 and 35 years now, and they live quite miserable and handicapped lives. One of them was treated with repeat neurosurgical resections alone (choroid plexus carcinoma), illustrating that such a result may also be the result of major surgical resection as well at the tumour disease itself, even without harmful effects of radiotherapy. In a 35-year survivor treated for posterior fossa anaplastic ependymoma in infancy, there was no residual tumour after resection, but she was treated according to protocol including craniospinal radiotherapy. During the first years, she was reasonably well-functioning, and hormonal substitution was given. In her teenage years, she could perform sheltered work, but over time, her development had a downhill course, with acute vascular episodes. She experienced major stroke several times, resulting in hemiparesis, and CT angiography demonstrated damage on major arterial structures and corresponding cerebral infarction (Fig. 1). The longest living infant treated with postoperative radiotherapy experienced another well-known complication; she underwent major resection of rapidly growing supratentorial meningiomas at the age of 26 and 35 years, and finally died 41 years old.

We understand that these depressing results can be considered to be ultimate consequences of a treatment that was abandoned approximately 30 years ago. Since late effects of radiotherapy were observed, particularly on immature brain, standard therapy was later modified. More modern protocols were introduced, including chemotherapy—and postponed, more targeted radiation. Our point is that evaluation of these new strategies is often discussed on the basis of survival figures, rather than quality of life. It is also true that serious long-term consequences for adult survivors from pediatric cancer are now more in focus, but long-term results are not specified for the infant group where the results could be expected to be most dramatic [3, 9].

Our small cohort illustrates that even the long-term results change over time, and that follow-up data should be reported also from perspective of 30–50-year survival and functional outcome and performance.

In contrary, the group of infants treated for low-grade tumours is a pleasure to meet as adults. This group is heterogeneous and the long-term results may obviously be influenced by the case-mix. It is perhaps not surprising to observe good results in patients with choroid plexus papillomas, astrocytomas, and other low-grade gliomas. In this small series of infants with low-grade tumours, all were treated with surgical resection alone, and only one child underwent repeat resections. This is in contrast to other low-grade series we have previously reported (from all pediatric patients regardless of age), where we have performed repeat resections instead of adjuvant treatment in case of local recurrence or progression of residual tumor [2, 4–7]. In the group of infants treated for low-grade tumours, 1-year survival was 88%. All these 15 patients are also among long-term survivors today (as adults aged from 20 to 43 years), and in fair clinical condition. They have all finished school, most of them unassisted, and they are in full activity. Four are students, and eight have normal employment and three are in part-time sheltered work. The working capacity for the whole group was better than expected. Several of the parents have spontaneously commented on the positive long-term result, which was much better than they expected and feared in the early years after treatment of their children.

Conclusion

The results from group of infants under 1 year of age treated for brain tumour in the period 1973–1998 are twofold.

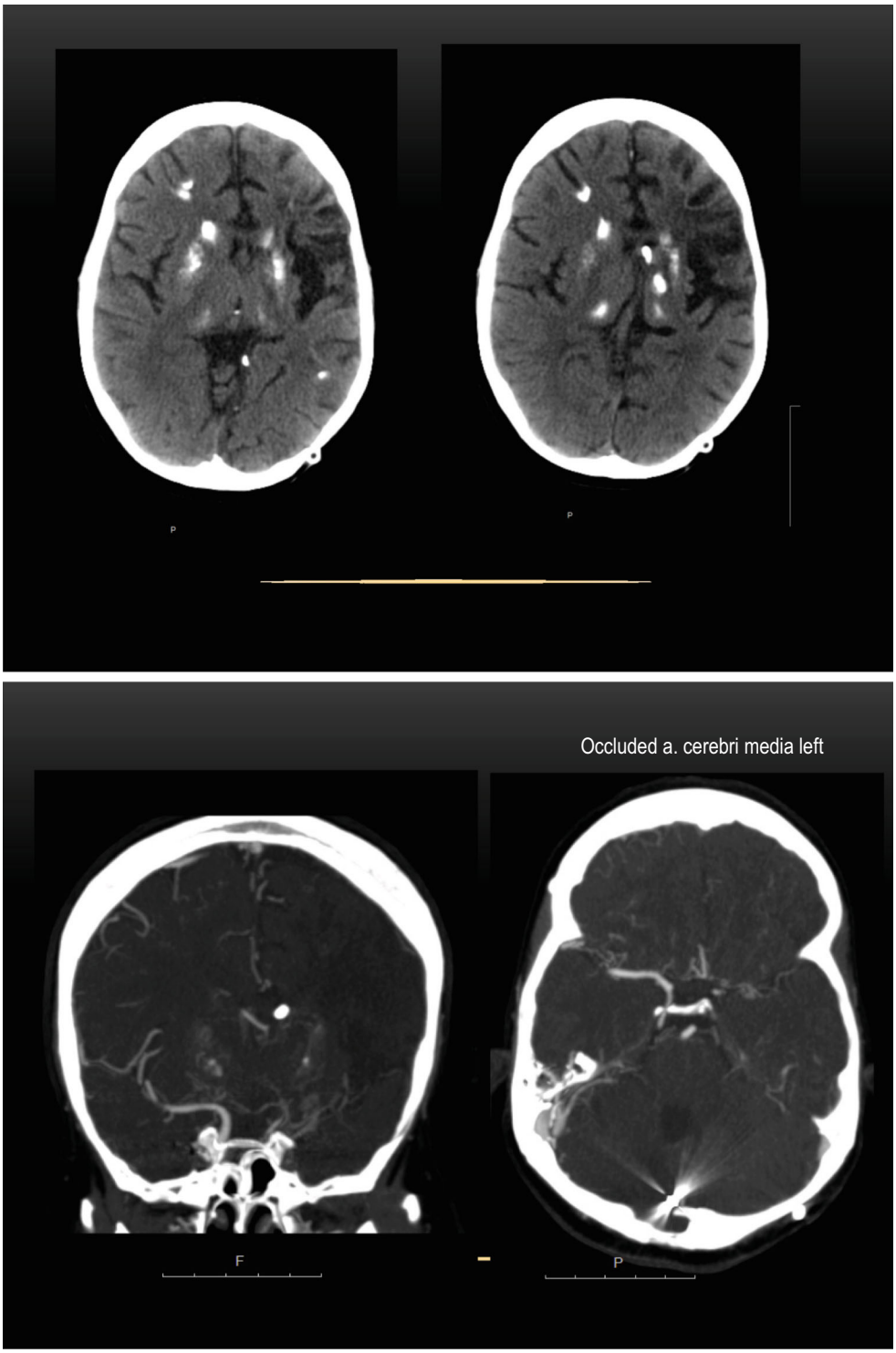

Fig. 1 CT and CT angiography in patient 12 (Table 1), taken 29 years after treatment demonstrating cerebral infarction (left middle cerebral artery territory) as well as damage of intracranial arteries—occluded left middle cerebral artery

While the results for the high-grade tumour group are depressing and even the long-term survivors experience a down-hill course as long as 20 to 40 years after initial treatment, we believe that this dismal course is in part due to late effects of radiotherapy, which is no longer in used in this age group today.

On the other hand, results from infants treated for low-grade tumours demonstrate a good functional outcome and working capacity 20 to 40 years after treatment. Since this patient group may include very different case-mix of low-grade tumours, results may differ considerably. This particular fact is important to

communicate when counseling parents of infants with brain tumours.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval For this type of study, formal consent is not required.

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