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Interdisciplinary treatment in pediatric patients with malignant CNS tumors

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Abstract Despite sophisticated surgical methods only a few pediatric CNS tumors can be controlled by operation alone. Therefore multimodality treatment regimens are needed to improve quality of life and survival, which is most important in malignant neoplasms. Since 1998 we have treated 16 children with malignant CNS tumors. All 16 patients have been treated on an interdisciplinary basis and are therefore accompanied by a pediatric neuro-oncology group consisting of a neurosurgeon, pediatric oncologist, and radiotherapist. Depending on tumor histology, child's age, and extent of surgery, further adjuvant therapy is planned by this group. Newly diagnosed tumors are typically treated by a specific chemotherapy protocol according to a multi-institutional study. In recurrent tumors more individual treatment regimens are considered. Data concerning surgery, adjunctive treatment, complications, and outcome of all patients and four case reports are presented.

Keywords Pediatric brain tumor · Malignant CNS tumors · Multimodality treatment · Chemotherapy · Radiation therapy

Introduction

Primary neoplasms of the CNS are the most common solid tumors in childhood, with an incidence of 2–5 per 100,000 per year [13]. Prognosis of these tumor entities still remains uncertain, although survival has been improved in recent years by better diagnostic and treatment facilities. Surgery and neuroanesthesia have become safer, and adjunctive treatment options offer new prospects. Prognosis still depends on the histological nature and location of the tumor. Despite sophisticated surgical methods only a few tumors can be controlled by operation alone. Therefore multimodality treatment regimens are needed to improve quality of life and survival, which is most important in malignant neoplasms.

Until 1980 standard treatment of malignant brain tumors consisted of surgery and radiation therapy. Only recurrent tumors were treated with chemotherapy as a palliative measure. In the subsequent two decades numerous chemotherapy protocols have been tested in different circumstances during treatment of pediatric brain tumors to define their true efficacy. Careful analysis of the results led to the definition of clear indications for adjuvant chemotherapy in some instances whereas in other conditions the chemotherapeutic efficacy remains uncertain. Radiation therapy is the most effective adjuvant treatment option in childhood brain tumors. New radiation technologies which allow small volume or focal irradiation while sparing surrounding tissue can help to minimize late effects in the developing nervous and skeletal

systems in at least some tumor entities. Today high-dose chemotherapy with autologous bone marrow transplantation or peripheral stem cell rescue and focal radiation therapies, for example, fractionated stereotactic radiotherapy (SRT) and stereotactic radiosurgery (SRS), provide children suffering from brain tumors greater chances of increasing quality of life and long-term survival.

From the neurosurgeon's point of view the technical standard has improved steadily over the past two decades. Stereoscopic microscopes with high magnification and illumination have been the most striking advance. Ultrasonic aspiration and laser techniques, such as the CO_2 laser in spinal tumor surgery have also proven important tools in ameliorating surgical outcome. Electrophysiological monitoring, neuronavigation systems, and perioperative imaging have substantially increased surgical safety. The best results regarding neurological outcome with a complete as possible tumor resection can be achieved when the neurosurgeon combines these sophisticated techniques with information obtained from excellent diagnostic pictures, and most recently by functional imaging. Finally for making decisions perioperatively in tumors of uncertain histology, immediate frozen-section assessment by the neuropathologist is very useful.

In addition to standard treatment protocols for certain newly diagnosed tumors, such as medulloblastomas, individual strategies for rare pathologies or recurrent diseases need to be defined. This occurs in neuro-oncological working groups consisting of pediatric neurosurgeons, pediatric oncologists, radiotherapists, and radiologists. Weekly conferences and aftercare programs for the patients in the respective outpatient departments are part of the quality control system that monitors the neurological status and radiological follow-up as well as endocrinological, ophthalmological, and neuropsychological findings.

Therapy

Surgery

In our department tumor surgery is planned electively whenever the child's clinical condition allows it in order to have time to perform sufficient preoperative imaging, planning of functional studies, and neuronavigation and to have available an experienced team of neurosurgeons and neuroanesthesiologists.

All patients with CNS tumors receive perioperative corticosteroids (dexamethasone), antibiotics (cefazoline), and additional anticonvulsants (phenytoin) in supratentorial lesions.

Craniectomy is no longer performed in posterior fossa surgery. We either open the skull by craniotomy or use polymethylmethacrylate. Spinal tumors are always approached by laminoplasty. If a dura substitute is necessary, we use material that normally does not cause scarring (Gore-Tex, W.L. Gore, Flagstaff, AZ, USA).

Deeply located tumors or lesions in eloquent regions are operated on with neuronavigation (frameless: BrainLab VectorVision; stereotactic frame: Zamorano-Dujovny unit, ultrasound). For most tumor entities the extent of resection is decisive for the prognosis [1, 5, 25]. Therefore perioperative resection control by ultrasound and postoperatively by early magnetic resonance imaging (MRI) allows more radical surgery and a second-look operation in single cases.

All patients with posterior fossa tumors are operated on in the prone or Concord position and receive an occipital external drainage in the same anesthetic. The decision for definite shunting is not made earlier than 10 days after tumor resection. We no longer shave patients and always use absorbable suture material.

Metastatic neoplasms are rare in childhood. In these instances surgery is the most effective treatment, except in secondary CNS lymphoma. Prognosis depends on primary disease.

Adjunctive treatment

Malignant supratentorial tumors in childhood have an unfavorable prognosis. Standard treatment has been surgery and adjunctive radiotherapy of the tumor bed [5]. In the past decade some combined chemotherapy regimens have shown a certain improvement in 5-year survival compared to adjunctive radiotherapy alone. In the recent past neoadjuvant and high-dose regimens with autologous bone marrow or peripheral stem cell rescue have been administered. Such strategies are still being evaluated. As in adult series, glioblastoma patients have the worst prognosis, followed by those with anaplastic astrocytomas. The effectiveness of adjuvant chemotherapy in these tumors is adversely affected by the blood-brain barrier and various other mechanisms, for example, the multidrug resistance gene, aldehyde dehydrogenase, and glutathione *S*-transferase [18]. Mixed gliomas and oligodendrogliomas have a significantly better prognosis than astrocytomas. They are also more sensitive to chemotherapy [4].

Optimal adjuvant treatment strategies for malignant supratentorial tumors have not yet been defined. Obtaining a sufficient number of study patients is difficult, due to the more heterogeneous tumor types and locations than in the more uniformly growing neoplasms of the posterior fossa, for example, those of the fourth ventricle. In older series the latter appeared to be more common than supratentorial neoplasms, but recent statistics show that more than 50% of CNS tumors are found in supratentorial regions [22].

Second tumors after previous radiotherapy, sometimes related to genetic syndromes are often located in the cerebral hemispheres [21].

Germinomas are generally nonsurgical tumors and can be treated by radiotherapy only [26].

The most common malignant solid neoplasms in childhood are *medulloblastomas*. These respond best to adjuvant radio- and chemotherapy [18, 19], although the extent of tumor resection still plays a dominant role in prognosis. Without adjuvant treatment, however, all patients die in 3 years [20]. High doses of craniospinal radiation double survival time, but significant late effects have resulted in efforts to reduce radiation doses. A recent study replaced standard craniospinal irradiation with 36 Gy by doses of 24 Gy, but due to a significant increase in failures the study was terminated [6]. In combination with chemotherapy dose-reduced radiotherapy seems to be equivalent to standard-dose irradiation. SRS is an option in small residual or local recurrent tumors, at least to minimize radiation sequelae [27].

In systemic recurrent disease high-dose chemotherapy with peripheral stem cell rescue or autologous bone marrow transplantation prolongs survival and may replace craniospinal irradiation in the future [2, 11].

For *ependymomas* macroscopically total tumor resection is the most important prognostic factor. However, adjuvant treatment appears to increase survival. Retrospective trials have shown postoperative radiotherapy significantly to improve outcome [23]. Local field irradiation with target volume doses up to 56 Gy seem to be the best modality since disseminated disease is rare (11%), even at relapse, and whole-brain and spin-axis radiotherapies produce more serious late effects. No randomized studies are available that confirm additional chemotherapy as being more effective than radiotherapy alone, but comparable results are found in infants treated with combination chemotherapy only. SRS and fractionated SRT are under investigation in local recurrent tumor. These modalities are tolerated well and may produce fewer side effects [10].

Malignant intramedullary spinal cord tumors have a bad prognosis, with a median postoperative survival of only 12 months. There is no confirmation of the effectiveness of adjunctive treatment, but since these tumors have an infiltrative character, the systemic treatment approach of radio- and chemotherapy seems to give these children a chance [3, 17].

Diffuse malignant glioma of the brainstem and basal ganglia cannot be managed by surgery. Few authors even recommend stereotactic biopsy in pons gliomas since all of them may take a malignant course, and biopsy specimens are not representative of the overall tumor. They also do not respond sufficiently to adjuvant radio- or chemotherapy. Radiotherapy has some effect on improving neurological deficits without affecting survival time [24].

Until 1980 standard treatment for pediatric brain tumors consisted of surgery alone and adjunctive radiotherapy in high-grade tumors or lesions that could not be resected due to localization or infiltrative growth. Growing experience in *chemotherapy* and concern about serious radiotoxicity in the developing nervous system have led to numerous trials testing the efficacy of chemotherapy regimens. Increased survival times in certain benign and malignant neoplastic diseases after chemotherapy help to reduce radiation doses, postpone the time of radiotherapy, and offer the prospect that in the future certain tumors may not need radiation therapy at all. Poor-risk groups with disseminated disease, only partially resected tumors, and younger patients benefit most from adjunctive chemotherapy [25].

New protocols are being used to investigate neoadjuvant chemotherapy in children younger than 3 years and in medium-risk medulloblastoma patients younger than 7 years [9, 15]. In recurrent disease high-dose protocols with peripheral stem cell or autologous bone marrow rescue show preliminarily good results [14]. Final evaluation of such strategies concerning long-term survival, control of disseminated tumor, and significant toxicity is not yet possible, but a toxic mortality rate of 20% in glioma patients has been reported [15, 18].

Other well known side effects are infections, hypacusis, neuropathy, tissue reactions such as fibrosis, calcification, and leukencephalopathy.

Radiation therapy is still the most effective adjuvant treatment in many CNS neoplasms in children pediatric and adults. In the pediatric population the widest experience has been with medulloblastoma radiotherapy. In this highly radiosensitive tumor 5-year survival rates have been increased to 70% by doses up to 60 Gy in the posterior fossa. Serious late effects must be considered, however, whenever such a therapy is carried out. Incomplete myelinization in children younger than 3 years leads to neurocognitive disorders; 90% of these children have an IQ below 90, and behavior disorders follow. Impaired growth due to hormonal insufficiency and direct damage to the spinal column in doses higher than 20 Gy are predictable. Previous radiotherapy is the most important cause of second tumors, mainly meningiomas and gliomas [1, 7, 8, 21].

Recent protocols with reduced or fractionated radiation doses have helped to minimize the side effects in surrounding tissues. Focal radiation techniques such as SRT or SRS are well tolerated since the surrounding brain is not substantially affected. The effects on highly sensitive structures in the vicinity of the radiation target, for example, the optic pathways and cranial nerves in general, and the hypothalamic-hypophyseal axis are still under investigation. Hyperfractionation (2×1 Gy daily) does not improve treatment [12]. Focal techniques are not likely to affect survival time because most of the tumors are disseminated or have an infiltrative character.

Radio- and chemotherapy administered together may potentiate their negative effects on skeletal growths and some toxic reactions, including lung fibrosis and leukencephalopathy.

Table 1 List of patients treated with a malignant brain tumor since 1998 [*T* tumor resection (95–100%), *ST* subtotal tumor resection (50–95%), *P* partial tumor resection (<50%), *SB* stereotactic biopsy, *TF* tumor free, *NP* no progression, *TP* tumor progression, *RT* recurrent tumor]

Patient no.	Sex	Age (years)	Operation	Radio	Chemo	Diagnosis	Outcome	Survival (months)
1	M	16	T	+	–	Ependymoma WHO III, recurrent	TF	52
2	M	3	T[d]	+	+	Medulloblastoma, recurrent	TF	29
3	F	9	P	+	+	Medulloblastoma	TF	14
4	F	4	T	+	+	Astrocytoma WHO III (spine)	TF	15
5	M	5	P	+	+	Filia (Ki1 lymphoma)	Death	1
6	M	5	T	+	+	Medulloblastoma	TF	21
7	M	8	SB (T)	+	–	Germinoma	TF	22
8	M	8	T	+	+	Medulloblastoma, recurrent	RT	61
9	M	4	T	+	+	Filia (neuroblastoma)	Death (TF)	13
10	M	12	T	+	+	Medulloblastoma	TF	24
11	F	5	T	+	+	Ependymoma WHO III, recurrent[a]	Death (TF)	19
12	F	9	T	+	+	Mixed glioma WHO III	TF	8
13	M	4	T	–	+	Medulloblastoma	TF	8
14	M	13	P	+[c]	+[c]	Astrocytoma WHO III[b]	Death	3
15	F	7	SB	+	+	Astrocytoma WHO III (thalamus)	NP	9
16	F	3	–	+	–	Pons glioma	TP	5

[a] Primary tumor ependymoma WHO II
[b] Second tumor after contralateral glioblastoma multiforme with complete remission
[c] Therapy after operation of primary tumor
[d] Primary tumor

Patients

Since 1998 we have operated on 16 children with malignant neoplasms of the CNS, four of them with recurrent brain tumors and two with metastatic manifestations after remission of the primary disease. In one little girl suffering from diffuse brainstem glioma and progressive neurological deficits we did not perform biopsy prior to the conformal radiotherapy due to the evident nature of the tumor (Table 1). All 16 patients were treated on an interdisciplinary basis, accompanied by a pediatric neuro-oncology group consisting of a neurosurgeon, pediatric oncologist, and radiotherapist. Boys were affected more often than girls (10:6) and the average age was 7 years. Eight children were younger than 7 years. Fifteen children received adjuvant radiotherapy. Thirteen were treated with additional chemotherapy. Of the 14 patients with primary CNS tumors, 9 are alive with no evidence of tumor, one has a nonprogressive residual tumor, and a 3-year-old girl suffering from a pons glioma shows clinically improvement after radiation. One patient developed a second recurrent tumor. One girl died because of a chemotherapy complication without evidence of tumor. One boy who had been treated successfully with surgery and adjuvant radio- and chemotherapy because of a glioblastoma 5 years previously developed a diffuse anaplastic astrocytoma in the contralateral hemisphere and died in tumor progression after partial resection without further treatment. Of the 11 surviving children who have been operated on 2 are suffering from residual ataxia and dysarthria in one case after a posterior fossa syndrome, and 9 are without neurological deficits. There have been no surgery-related infections or healing disorders. Survival time in is 1–61 months.

The following cases are representative of individual interdisciplinary treatment planning.

Case 1 (patient 8)

An 8-year-old boy had been operated on for a medulloblastoma of the fourth ventricle at the age of 5 years. Postoperative MRI showed no residual tumor or neurological deficits. Adjuvant chemotherapy and craniospinal radiotherapy with posterior fossa boost followed. Routine craniospinal MRI carried out 34 months after resection of the primary tumor revealed a small contrast-enhancing lesion in the roof of the right lateral ventricle and suspective signal changes in vertebrae C4–C6. The results of ^{111}In-labeled octreotide scintigraphy were positive for the ventricular but not for the bony lesions. When the ventricular lesion showed macroscopic growth, it was removed. Histological examination confirmed a medulloblastoma. In the same anesthesia an Ommaya reservoir for potential intrathecal chemotherapy was inserted and computed tomography guided biopsy specimens were taken from vertebral body C5 excluding further metastatic tumor.

Again he recovered well without neurological deficits. After the second surgery he was treated with a high-dose chemotherapy and peripheral stem cell rescue and thereafter received a radiation boost to the tumor bed (Fig. 1). Fifteen months after the second operation he again developed tumor recurrence. This time a multifocal spread inside the right lateral ventricle was diagno-

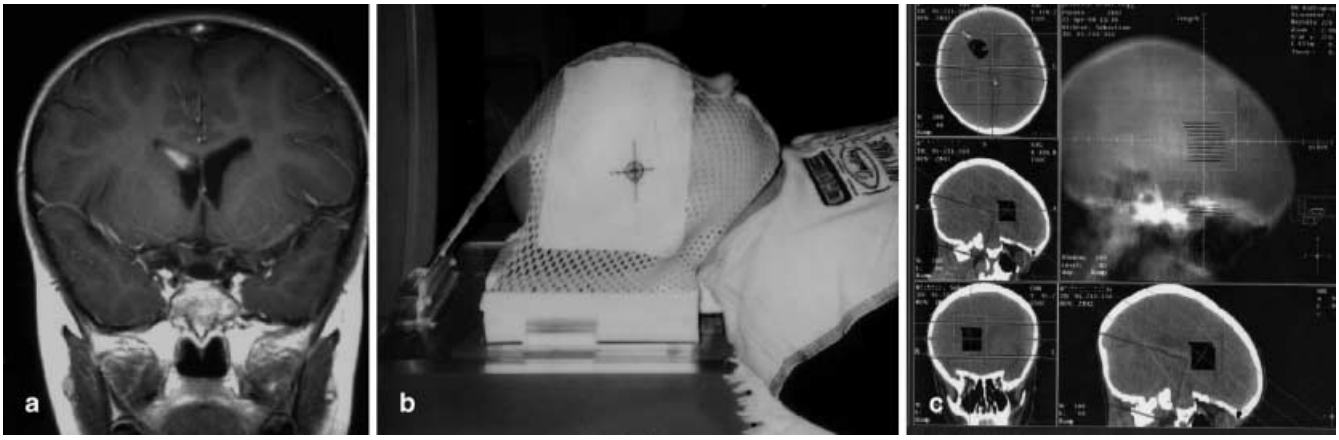

Fig. 1 a Gadolinium-enhanced T1-weighted MRI with recurrent medulloblastoma in lateral ventricle. **b** Positioning and immobilization in head mask for local fractionated radiotherapy. **c** Reconstructed axial, sagittal, and coronal views showing radiotherapy planning

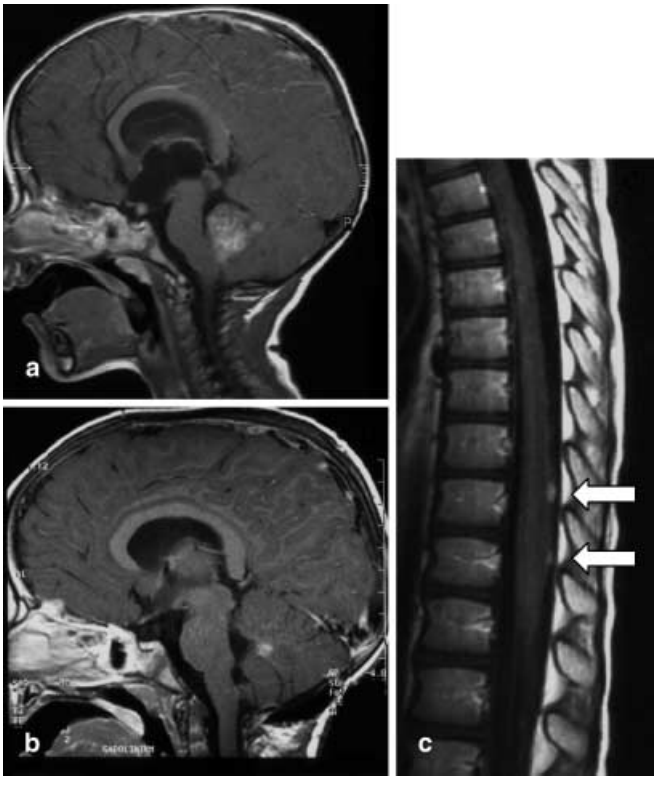

Fig. 2 a Gadolinium-enhanced T1-weighted MRI of primary medulloblastoma of the fourth ventricle. **b** Local recurrent tumor. **c** Spinal dissemination at level T10–T12

sed. He was put on a third chemotherapy protocol with stem cell support, which he still tolerates well.

Upon beginning school at the age of 6 years he developed learning problems. His growth curve dropped below the 3rd percentile 3.5 years after craniospinal radiotherapy, and he is suffering from cisplatinum-induced hypacusis.

Treatment data

Surgery. First operation (November 1994): prone position, craniectomy and C1 arch resection, microsurgical tumor removal (fourth ventricle). Second operation (January 1998): stereotactically guided microsurgical tumor removal (right lateral ventricle), Ommaya reservoir implantation. Computed tomography guided biopsy specimens taken from vertebral body C5.

Chemotherapy. First treatment (November 1994–February 1995), sandwich arm: ifosfamide, etoposide, methotrexate, cisplatinum, cytosine arabinoside [German Society of Pediatric Oncology and Hematology (GPOH) protocol, HIT 91). Second treatment (February 1998): high-dose busulfan, thiotepa, peripheral stem cell rescue (Kalifa protocol). Third treatment (since April 1999): carboplatinum, etoposide (intravenous and intrathecal), stem cell support (GPOH protocol HIT–Rezidiv 92).

Radiotherapy. First treatment (March 1995–April 1995): neuraxis 35.2 Gy (5×1.6), neurocranium 35.2 Gy (5×1.6), boost 20 Gy (5×2), total 55.2 Gy. Second treatment (May 1998–March 1998): boost tumor bed 19.5 Gy (5×1.5), total 54.7 Gy

Case 2 (patient 2)

At the age of 2.7 years the boy presented with typical signs of increased intracranial pressure, and a medulloblastoma of the fourth ventricle was diagnosed. Total resection of the tumor mass was carried out. Postoperative craniospinal MRI showed no residual tumor mass or metastases. The postoperative course was unremarkable without neurological deficits. Definitive shunting had to be performed because he did not tolerate closure of the

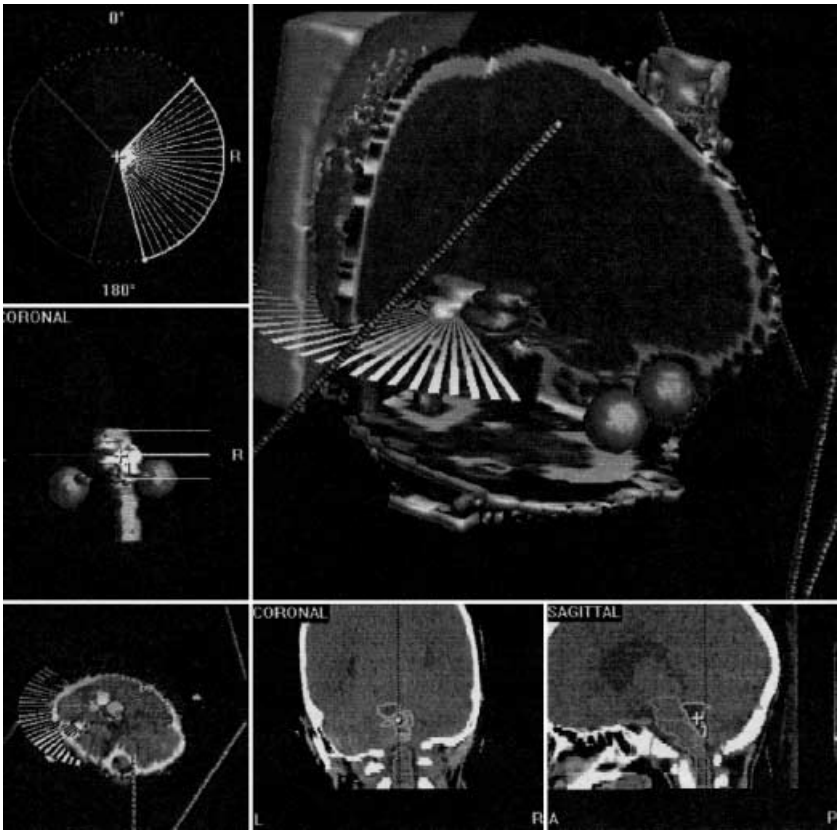

Fig. 3 Three-dimensional SRT planning for tumor boost in fourth ventricle demonstrates target, optic chiasm, and one arc. The dose distribution is shown in reconstructed sagittal and coronal views

external drainage. An Ommaya reservoir was implanted during the same session for intrathecal therapy followed by a chemotherapy protocol for babies. Twelve months postoperatively he developed asymptomatic multifocal tumor recurrence in the fourth ventricle and thoracic spinal canal (Fig. 2).

He was put under a second high-dose chemotherapy protocol with peripheral stem cell rescue. Complete remission was achieved for 54 days. CSF puncture was then tumor cell positive, and consolidation radiotherapy with reduced craniospinal dose and SRT in the posterior fossa (Fig. 3) was initiated, followed by an additional boost to the spinal cord (T10–T12). MRI showed complete tumor remission.

The clinical course was unremarkable, despite massive ascites 11 months after the beginning of the first chemotherapy course. Laparotomy with biopsy of the cyst walls did not reveal chronic infection or tumor cells. The cause remained uncertain; an unspecific reaction to intrathecal methotrexate therapy and distribution by the ventriculoperitoneal shunt have been discussed. The problem resolved spontaneously.

Treatment data

Surgery. First operation (September 1997): Concord position, external drainage, craniectomy, microsurgical tumor removal (fourth ventricle), cranioplasty (polymethylmethacrylate); delayed ventriculoperitoneal shunt (δ I) and Ommaya reservoir implantation. Second operation (June 1998): explorative laparotomy and cyst biopsy.

Chemotherapy. First treatment (July 1997–March 1998): methotrexate (intravenous and intrathecal), cyclophosphamide, carboplatinum, etoposide, vincristine (GPOH protocol HIT–SKK 92). Second treatment (July 1998): high-dose busulfan, thiotepa, peripheral stem cell rescue (Kalifa).

Radiotherapy. Treatment (April 1999–June 1999): neuraxis 32 Gy (5×1.6), neurocranium 32 Gy (5×1.6), SRT boost 18 Gy (5×1.8), total 50 Gy. Spinal boost (T10–T12) e^{-6} MeV (4×2), total 40 Gy (Figs. 1, 2).

Case 3 (patient 4)

A 4-year-old girl with chronic neck pain was first treated orthopedically. After additional vomiting cerebrospinal MRI was performed, and an intramedullary tumor C3–C7 was diagnosed. Complete surgical removal was carried out without neurological deficits (Figs. 4, 5). Postoperatively the parents observed an increase in the child's physical and psychomotor activities. Laminoplasty healed

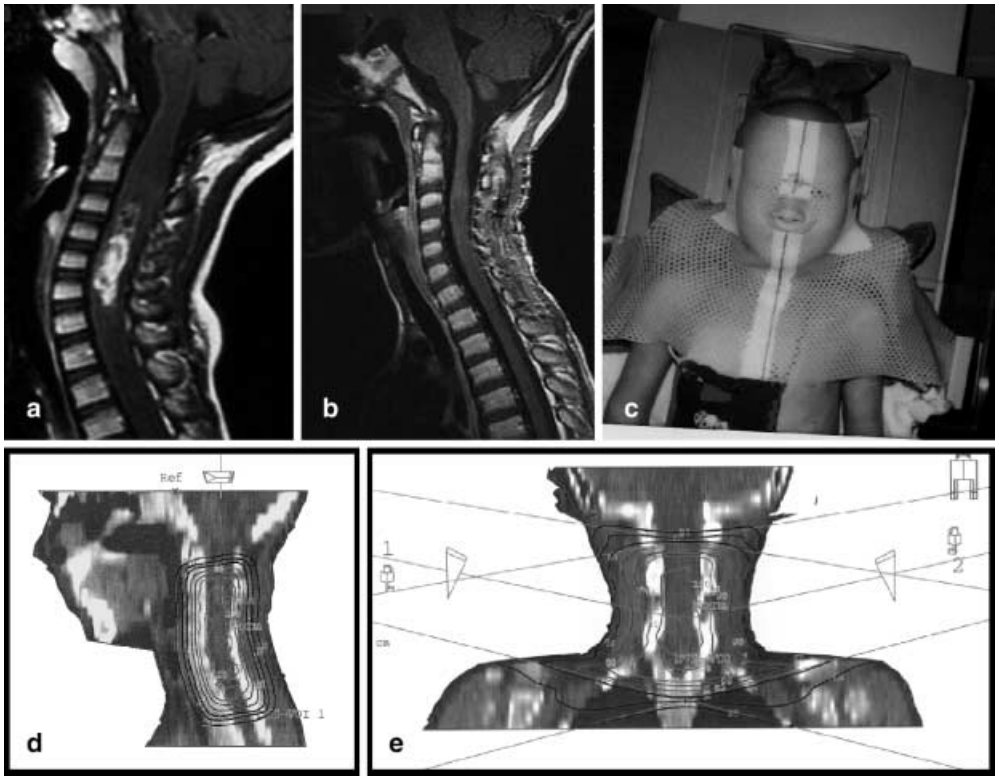

Fig. 4 Gadolinium-enhanced MRI demonstrating an intramedullary anaplastic astrocytoma at C3–C7. **a** Preoperatively, **b** postoperatively. **c** Positioning of the patient, immobilization mask, and vacuum mattress for three-dimensional fractionated radiotherapy. **d**,**e** Reconstructed sagittal (**d**) and coronal (**e**) views with dose distribution optimized by wedge filters

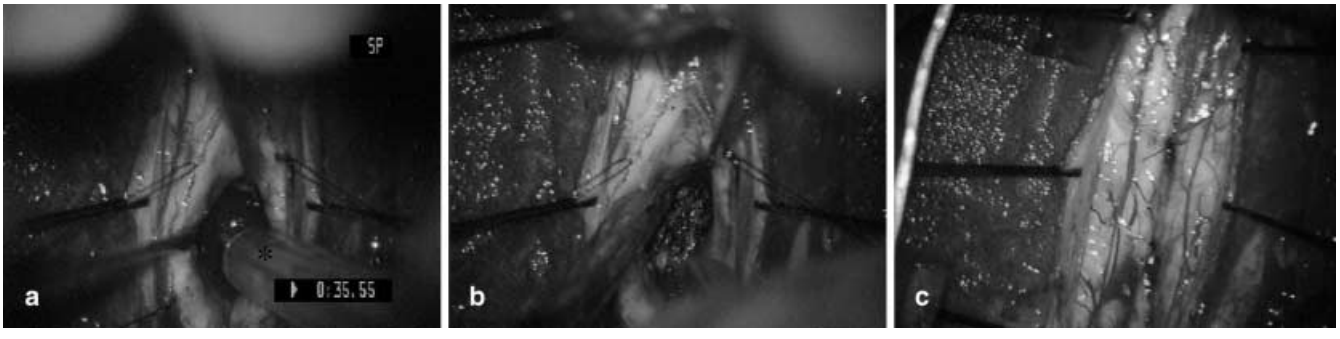

Fig. 5 **a** Surgery of intramedullary anaplastic astrocytoma; *asterisk* tumor reduction by ultrasonic aspirator, **b** Coagulation of the tumor bed with CO_2 laser. **c** Readaptation of myelotomy edges

without complication. The girl had worn a Philadelphia collar for 8 weeks. The tumor was classified histologically as anaplastic astrocytoma (WHO grade III), and adjuvant therapy became necessary. Due to the child's age chemotherapy was performed first, followed after 12 cycles by radiation therapy. MRI prior to radiation showed no visible tumor. The neurological and functional condition of the cervical spine is excellent. The only complication has been hypacusis due to cisplatinum.

Treatment data

Surgery. Operation (September 1998): Prone position, laminoplasty C2–C7 (fluoroscopy assisted), microsurgical tumor removal, longitudinal myelotomy and coagulation with CO_2 laser, tumor mass reduction with ultrasonic aspirator.

Chemotherapy. Treatment (October 1998–June 1999): cisplatinum (replaced by carboplatinum because of hypacusis), etoposide, lomustine (Chastagner and Kalifa protocol, modified International Society of Paediatric Oncology phase II)

Radiotherapy. Treatment (July 1999–August 1999): three-dimensional conformal radiotherapy to the cervical spine 30 Gy (1.5×5) with two optimized fields

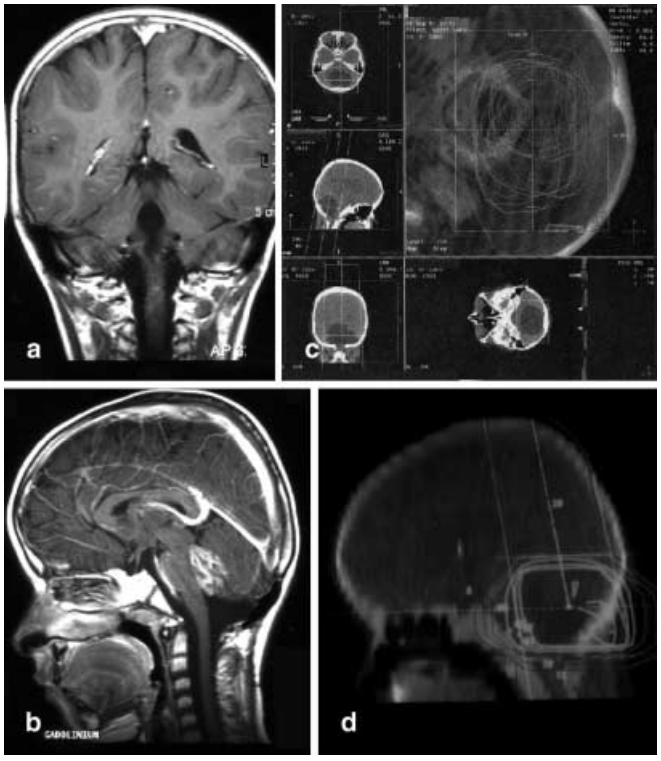

Fig. 6 **a**,**b** Gadolinium-enhanced T1-weighted MRI after resection of an extensive ependymoma in the posterior fossa (**a**) and demonstrating recurrent tumor (**b**) in the radiation field 12 months after radiotherapy. **c**,**d** Reconstructed images in axial, sagittal, and coronal views showing dose distribution

Case 4 (patient 11)

At the age of 4 years the little girl was operated on for an ependymoma (WHO grade II) of the fourth ventricle with extension into the aqueduct, subarachnoid space, and down to C2. Postoperative craniospinal MRI showed no residual tumor or metastases. The neurological status was normal. Persisting occlusive hydrocephalus was treated with a ventriculoperitoneal shunt. Postoperative focal radiation therapy of the posterior fossa was well tolerated. Eleven-months after the first operation MRI still detected no tumor. The next routine investigation after another 3 months showed a rapidly growing recurrent tumor mass in the fourth ventricle (Fig. 6). The girl was operated on again, with macroscopically total tumor resection. Left-sided facial palsy resulted from tumor infiltration into the rhomboid fossa. This time the tumor was classified as anaplastic ependymoma (WHO grade III) and adjuvant chemotherapy was initiated. After five cycles the girl died of atypical pneumonia 19 months after primary diagnosis. The causative organism remained unknown. At that time she was in complete remission.

Treatment data

Surgery. First operation (August 1997): Concord position, external drainage, craniectomy, microsurgical tumor removal, dura substitute (Gore-Tex), cranioplasty (polymethylmethacrylate), definitive ventriculoperitoneal shunting (δ level II). Second operation (October 1998): Concord position, microsurgical tumor removal.

Chemotherapy. Treatment (October 1998–June 1999): cisplatinum, etoposide, lomustine (Chastagner and Kalifa, modified International Society of Paediatric Oncology phase II).

Radiotherapy. Treatment (September 1997–October 1997): local tumor bed, 54 Gy (1.5×5), after 45 Gy reduction in target volume.

Discussion

Most of the malignant brain tumors in childhood are biologically systemic diseases of the CNS, although imaging typically demonstrates focal lesions. In these cases the neurosurgical approach can solve only the focal problem, and does not control the further course. However, successful adjuvant therapies depend on maximum surgical cytoreduction.

In our recent surgical series (Table 1) we achieved total (95–100%) tumor resection in malignant primary CNS neoplasms in nine patients (70%). In the other four cases two partial resections (extensively disseminated medulloblastoma and second CNS malignancy in precentral area) and two stereotactic biopsies (germinoma and thalamic astrocytoma) were performed. Surgical outcome was excellent in 11 patients (73%) without neurological deficits and surgery-related complications. The four remaining children showed ataxia and dysarthria, one posterior fossa syndrome, one facial palsy in a recurrent ependymoma, and one child had already been in a moribund state preoperatively due to systemic lymphoma.

Depending on tumor histology, the child's age, and extent of surgery further adjuvant therapy is planned by the pediatric neuro-oncology group. All CNS neoplasms operated on at our institution are histologically classified by the local neuropathologist and the German Reference Center of Neuropathology in Bonn (O. Wiestler). Newly diagnosed tumors are typically treated by a specific chemotherapy protocol according to a multi-institutional study. In recurrent tumors more individual treatment regimens are considered.

In medium-risk medulloblastoma patients we try to defer radiotherapy until the child reaches 7 years. Children with failing tumor control under chemotherapy or malignant gliomas require radiotherapy earlier.

Whenever possible we try to perform focal radiotherapy, such as stereotactic fractionated radiotherapy, in or-

der to spare nonaffected brain tissue. Fractionation in all radiation techniques is a very important protective factor for the developing brain, especially the white matter. In SRT precise and reproducible fixation of the target organ is mandatory. Our patients are immobilized in head masks and vacuum mattresses, which are tolerated well and do not need anesthetic, even in small children (patient nos. 2 and 4, both 4 years old).

We feel that continuous interdisciplinary discussion during the entire treatment course of a child suffering from a malignant CNS tumor is essential for an optimal result in terms of quality of life and survival time. Typical or unexpected complications and recurrent tumors often make changes in therapeutic strategies necessary, and all aspects must be considered in the interdisciplinary group. Each specialist knows best about the specific risks in his field.

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