Acta Neuropathol (1996) 91 : 578–586

REGULAR PAPER

Bettina Behring · Wolfgang Brück · Hans H. Goebel
Julianne Behnke · Arnulf Pekrun
Hans-Jürgen Christen · Hans A. Kretzschmar

Immunohistochemistry of primary central nervous system malignant rhabdoid tumors: report of five cases and review of the literature

Received: 13 March 1995 / Revised: 25 September 1995 / Revised, accepted: 21 November 1995

Abstract Malignant rhabdoid tumors (MRT) are characterized by a typical light microscopic morphology with uniformly round tumor cells, vacuolated cytoplasm with occasional round, hyaline intracytoplasmic, periodic acid-Schiff-positive inclusions, vesicular nuclei with prominent nucleoli and positive immunoreactivity for vimentin. The histogenesis of MRT is controversial. Five cases of primary central nervous system (CNS) rhabdoid tumors in children are presented. Immunohistochemical, light and electron microscopic features are compared with primary CNS malignant rhabdoid tumors reported in the literature. Expression of various neurofilaments in our cases of primary CNS rhabdoid tumors was prominent and we therefore favor a neural differentiation of extrarenal intracerebral rhabdoid tumors.

Key words Malignant rhabdoid tumor · Immunohistochemistry · Central nervous system

Introduction

Malignant rhabdoid tumor (MRT) is a rare embryonal neoplasm originally described in the kidney as a rhabdomyosarcomatoid subtype of Wilms' tumor [4]. It was later identified as a tumor entity with characteristic ultrastructural features distinct from Wilms' tumor [19]. The term "rhabdoid" was chosen because the light microscopy findings were strongly suggestive of myoblastic differentiation; however, the immunohistochemical and ultrastructural findings do no support a muscle cell origin. The histogenesis of this tumor is yet unclear. On the one hand, a mesenchymal origin of the tumor was suggested by Biggs et al. [5] based on the variety of primary sites of occurrence and on the presence of aggregated vimentin filaments in tumor cells. On the other hand, a neuroectodermal cell origin of rhabdoid tumors is suspected due to their association with embryonal brain tumors [6]. Rhabdoid tumors are known to occur in the kidney without any second tumors in other locations; they are also more rarely found to be associated with additional primary neuroglial tumors in the midline posterior fossa [6]. MRT may also be primarily located in the central nervous system (CNS). This report presents neuropathological and immunohistochemical findings in five patients with primary malignant rhabdoid tumors in the CNS. Findings of other immunohistochemical studies of primary CNS malignant rhabdoid tumors are compared with our results.

B. Behring · W. Brück · H. A. Kretzschmar (✉)
Institute of Neuropathology, University of Göttingen,
Robert-Koch-Strasse 40, D-37075 Göttingen, Germany
Tel.: 49 551-392700; Fax: 49 551-398472

H. H. Goebel
Department of Neuropathology, University of Mainz,
Mainz, Germany

J. Behnke
Department of Neurosurgery, University of Göttingen,
Göttingen, Germany

A. Pekrun
Department of Pediatrics, University of Göttingen,
Göttingen, Germany

H.-J. Christen
Department of Neuropediatrics, University of Göttingen,
Göttingen, Germany

Material and methods

Case reports

The pathological findings in five patients, and in one case an additional recurrent tumor, are reported. The diagnosis of MRT was established by light and electron microscopy and immunohistochemistry following partial or total tumor resection.

Case 1

At the time of diagnosis the patient, a 2-year 3-month-old girl, had developed increased intracranial pressure caused by a large fronto-temporo-parietal brain tumor in the parenchyma of the left hemisphere, attached to the tentorium. There was no evidence of an extracranial tumor. At surgery only incomplete resection was possible due to the close vicinity of the tumor to thalamic structures. Af-

ter a first course of chemotherapy according to the German Society of Pediatric Oncology (GPO)-protocol (HIT, procarbazine, ifosfamide, VP16, methotrexate, cytosine-arabinoside, cisplatin), the residual tumor was removed 3 months after the first operation. After the second round of chemotherapy and additional craniospinal irradiation (35 Gy and local boost 20 Gy) the patient showed no neurological symptoms. There was also no radiological evidence of residual tumor. At 1 month after completion of the chemotherapy and radiotherapy the child again complained of headaches, nausea and vomiting. A cerebral computed tomogram (CT) showed a large parieto-temporal tumor of the left hemisphere. She died 4 weeks later, 11 months following the initial diagnosis of the tumor.

Case 2

This patient was a 5-year 3-month-old girl who developed headaches, vomiting and signs of palsy of the left forth cranial nerve. One month after the onset of clinical signs magnetic resonance (MR) and CT imaging showed a large tumor located intraparenchymatously in the right cerebellar hemisphere, infiltrating the foramina Luschkae, with no signs of intracranial or extracranial metastases. After incomplete surgical removal of the tumor, cytostatic therapy was performed, similar to the treatment of patient 1. In addition the patient received craniospinal radiotherapy with a dosage of 24 Gy and a local tumor boost of 30 Gy. There was no clinical or radiological evidence of residual tumor. After a period of 8 months without symptoms, the tumor was found to have spread along the subarachnoid space and the patient died 1 month later.

Case 3

This patient, an 8-month-old boy, developed vomiting, muscle hypotonia and loss of consciousness within only a few days. CT scan revealed a large brain tumor located in the left temporo-parietal hemisphere causing a midline shift to the right. There were no signs of extracranial malignant tumor or metastases. The tumor was resected without visible residue. After a 2-month period with no clinical symptoms the patient developed signs of tumor relapse which was confirmed by CT scan. A second operation was performed leading to surgical resection of the tumor which was firmly attached to the dura mater. The patient recovered from the second operation without gross neurological anomalies. Two weeks later intensive cytostatic therapy was begun according to the brain tumor study protocol of the GPO, similar to the treatment for patient 1. The therapy was well tolerated. The patient received craniospinal radiotherapy with a dosage of 35.2 Gy and a local tumor boost (20 Gy). Three months later neurological and radiological examinations revealed a second tumor relapse at the original site. The patient died at the age of 18 months, 10 months after the first surgical tumor removal.

Case 4

This boy was 1 year 10 months old at the time of neurosurgical tumor resection. Two months before surgery he had developed vomiting, weight loss and progressive deterioration, and later a complete inability to walk. An intraspinal tumor located between T11/12 and L3/4 was found. There was no evidence of extracranial or intracranial metastases or other tumors at that point of time. The tumor was subtotally resected. The patient underwent chemotherapy (similar to the treatment of patient 1) and radiation (CNS radiation with 30 Gy, tumor boost with 20 Gy). One month after completion of the therapy the boy regained the ability to walk and showed no neurological symptoms. Follow-up sonographies of the spinal medulla and the internal organs, especially the kidneys, revealed no recurrent tumor or metastases. About 1.5 years after the spinal tumor resection he developed meningism and vomiting. A cranial CT revealed a brain stem tumor with brain stem compression and hydrocephalus internus. The entire spinal cord was free of recurrent tumor or metastases. The brain tumor was interpreted as a metastasis of the spinal malignant rhabdoid tumor. After rapid clinical deterioration the child died 2 days later, shortly before surgery and 1.5 years after the intraspinal rhabdoid tumor had been diagnosed.

Case 5

This 4-month-old girl developed vomiting, gaze deviation to the left and a slight hyperreflexia of the left side for 2 days. CT and MR imaging showed a large intraparenchymatous tumor of the left hemisphere causing a midline shift to the right. There were no signs of extracranial malignant tumor or metastases, particularly not of the kidneys. Three days after the onset of clinical signs the tumor was partially removed. Postoperatively, the child developed a strong opisthotonus, hyperreflexia, extrapyramidal signs, wide pupils with slow reactivity, hyperactivity and hyperexcitability. Cerebral CT controls 3 and 6 months after the neurosurgical operation revealed a massive progression of the left tumor with a massive hydrocephalus internus occlusus. The child showed progressive deterioration of the neurological symptoms. In October 1995, at the age of 13 months, she died at home, 9 months after the diagnosis and operation of the rhabdoid tumor.

Light microscopy and immunocytochemistry

For light microscopy fresh tumor tissue was fixed in 4% neutral buffered formalin and processed routinely for paraffin embedding. Sections of 3–4 μm were stained with hematoxylin and eosin, elastica van Gieson, Gomori reticulin and PAS. For immunohistochemistry routinely fixed and processed paraffin-embedded tissue was used. Tissue sections were deparaffinized, rinsed in phosphate-buffered saline (PBS and incubated for 1 h at room temperature with primary antibodies to vimentin (monoclonal, 1:1, H. Biermann GmbH), glial fibrillary acidic protein (GFAP; monoclonal, 1:1, H. Biermann GmbH), neurofilament protein (NF) 68 kDa, 160 kDa, and 200 kDa (monoclonal 1:400, Sigma), neuron-specific enolase (NSE; monoclonal, 1:1, Amon), synaptophysin (monoclonal, 1:20, Dako), cytokeratin (KL1 monoclonal, 1:1, H. Biermann GmbH), desmin (monoclonal, 1:1, Dianova), anti-smooth muscle actin (monoclonal, 1:1, Dianova) [39], epithelial membrane antigen (EMA; monoclonal, 1:1, H. Biermann GmbH), S-100 protein (S100; monoclonal, 1:1, H. Biermann GmbH), and alpha-fetoprotein (AFP; polyclonal, 1:1, Dianova) in PBS containing 0.1% bovine serum albumin (BSA). After washing with PBS the slides were incubated with secondary rabbit anti-mouse antibody in PBS and BSA for 1 h at room temperature, and with alkaline phosphatase-anti-alkaline phosphatase (APAAP) for 1 h in PBS and BSA at room temperature followed by a 30-min incubation in Neufuchsin, rinsing in water and mounting with gelatine.

Frozen material was available from two of our cases. Sections of these tumors were stained with an antibody against neural cell adhesion molecule (NCAM, CD56, Dianova, Hamburg, Germany). The staining procedure was the same as described above.

Electron microscopy

For electron microscopy fresh tissue was fixed in 3% glutaraldehyde in PBS and post-fixed in 1% phosphate-buffered osmium tetroxide. Following dehydration in graded alcohols and propylene oxide, tissue blocks were embedded in Araldite and cut on an ultramicrotome. Ultrathin sections were double-stained with uranyl acetate and lead citrate and examined with a Zeiss EM 10 B electron microscope. All cases presented here were studied ultrastructurally. Since the morphology was similar in all cases, the ultrastructure of only one tumor is given as an example.

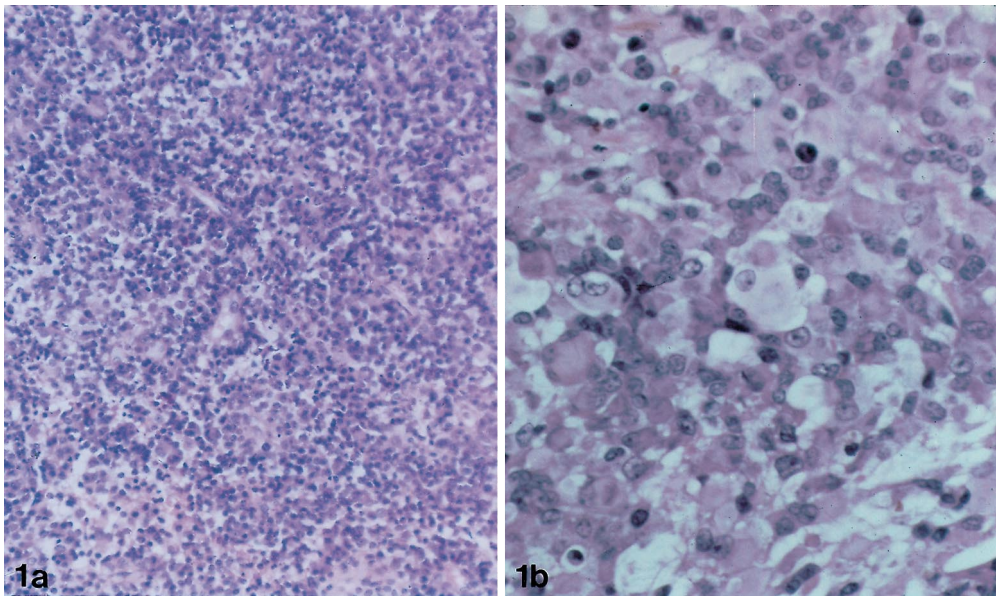

Fig. 1 a, b The tumor is composed of uniformly round tumor cells with vacuolated cytoplasm. **a** Case 5, **b** case 1; **a, b** H&E; **a** × 100, **b** × 250

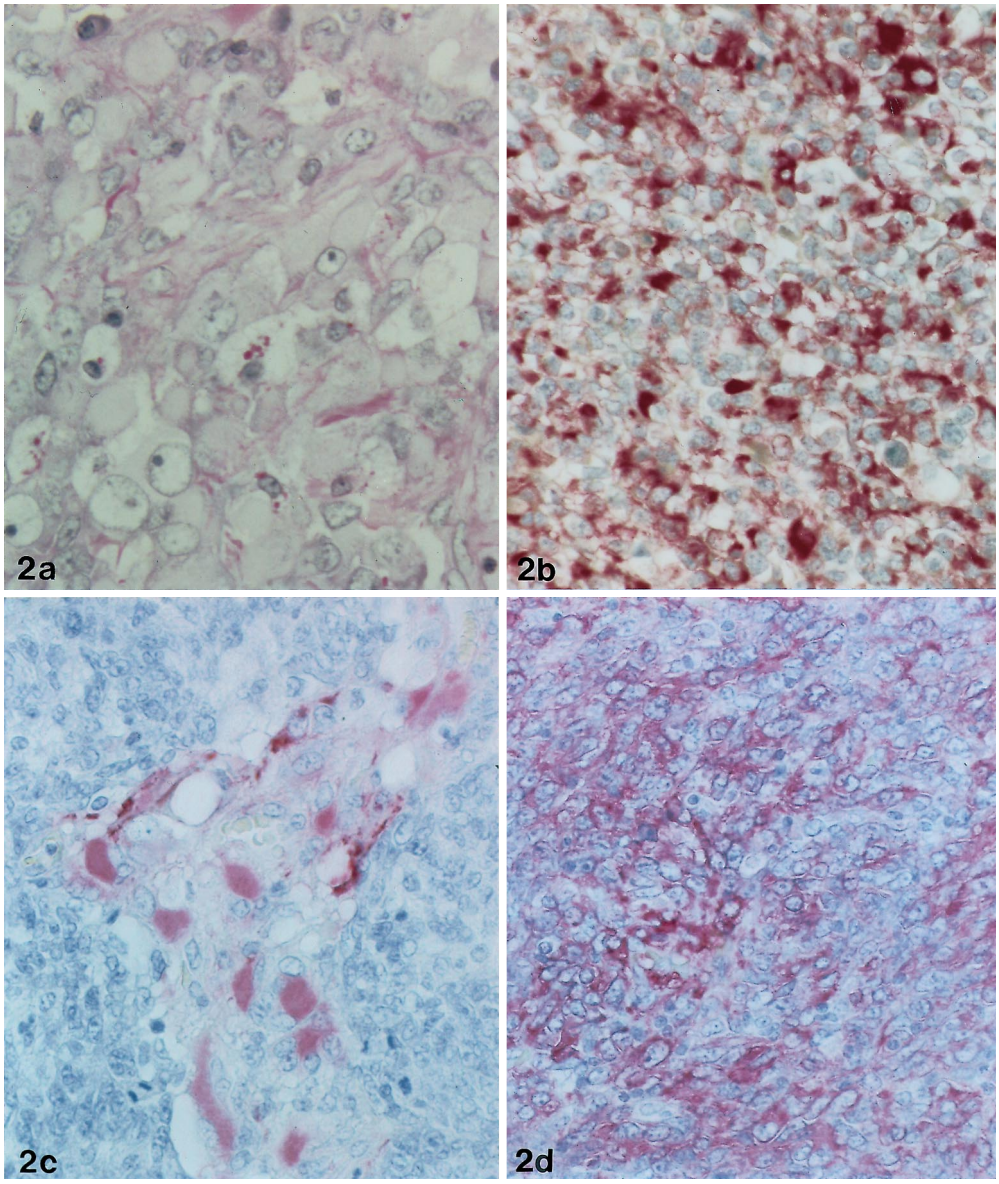

Fig. 2 **a** Case 1: Occasional round, hyaline intracytoplasmic, PAS-positive inclusions are found. **b** Case 2: Many tumor cells are positive for vimentin. **c** Case 3: Single tumor cells express GFAP. **d** Case 3: Most tumor cells are positive for actin. **a–d** × 250

Table 1 Immunohistochemical findings in five cases of primary malignant rhabdoid tumors of the central nervous system. Values indicate: 0, no tumor cells positive; X, less than 10% of tumor cells positive; XX, 10–50% of tumor cells positive; XXX, more than 50% of tumor cells positive; n.a., no frozen material available (*AFP* α-fetoprotein, *CK* cytokeratin, *EMA* epithelial membrane antigen, *GFAP* glial fibrillary acidic protein, *NF 68, 160, 200* neurofilament 68 kDa, 160 kDa, 200 kDa, *NSE* neuron-specific enolase, *S100* S-100 protein, *SYN* synaptophysin, *VIM* vimentin, *NCAM* neural cell adhesion molecule)

	VIM	NF 68	NF 160	NF 200	NSE	SYN	GFAP	Actin	Desmin	EMA	CK	S100	AFP	NCAM
Case 1														
Primary	XXX	XX	XXX	XX	XX	0	X	X	0	X	X	XX	0	0
Recurrent	XXX	XX	XXX	XXX	0	0	X	X	0	0	X	0	0	n.a.
Case 2	XXX	X	XXX	XX	0	0	0	XX	0	X	X	X	0	n.a.
Case 3	XXX	X	XX	XX	0	0	X	XXX	0	0	X	0	0	n.a.
Case 4	XXX	X	XXX	XX	0	0	0	X	0	0	0	XX	0	n.a.
Case 5	XX	XXX	XX	XXX	XX	0	X	X	0	X	XXX	XX	X	XX

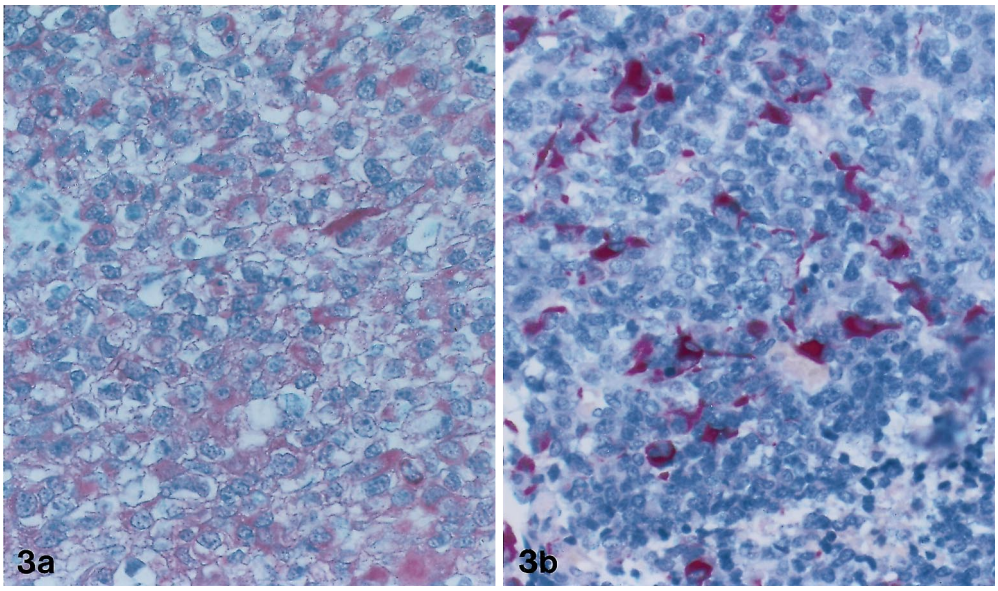

Fig. 3 **a** Case 2: The neurofilament protein 160-kDa subtype is expressed by numerous tumor cells. **b** Case 5: Many cells reveal positivity for the neural cell adhesion molecule. **a, b** × 250

Results

Light microscopy

Microscopically, MRT showed mainly diffuse cellular sheets of undifferentiated cells. The round or polygonal cells had sharply defined cell membranes. The nuclei were highly polymorphic, ranging from small hyperchromatic to larger irregular nuclei with nearly vesicular karyoplasm. The nuclei were often eccentric and contained a prominent central nucleolus. The tumor cells varied significantly in size. There were abundant small, round, undifferentiated tumor cells, but also a population of larger polygonal cells with abundant eosinophilic cytoplasm (Fig. 1 a, b). The cytoplasm was abundant, eosinophilic and contained hyaline, spherical, paranuclear intracytoplasmic inclusions which displaced and sometimes indented the nucleus. The inclusions were PAS positive (Fig. 2 a). Some fields of the tumors displayed more pleomorphic nuclei. There were fine strands of collagenous tissue running through the tumor. Numerous mitotic figures and some multinucleated cells were also present. Necrosis was present in all tumors. Vascular endothelial proliferation was not seen.

Immunohistochemistry

A variety of immunohistochemical stains were performed on paraffin-embedded tissue from surgical specimens and are summarized in Table 1.

Areas of vimentin immunoreactivity were the most consistent finding: immunohistochemical stains of cases 1 a/b, 2, 3, 4 and 5 showed cytoplasmic immunoreactivity in most of the tumor cells particularly in the large polygonal cells with hyaline intracytoplasmic inclusions (Fig. 2 b).

All tumors also expressed different NF (68 kDa, 160 kDa, and 200 kDa) in various amounts (Fig. 3 a). NF were expressed in many tumor cells with the most prominent expression in the small cell population described above. Of the examined cases 1 a and 5, case 5 was moderately positive for the NCAM (Fig. 3 b). Other neural markers were only expressed in parts of some tumors: NSE was

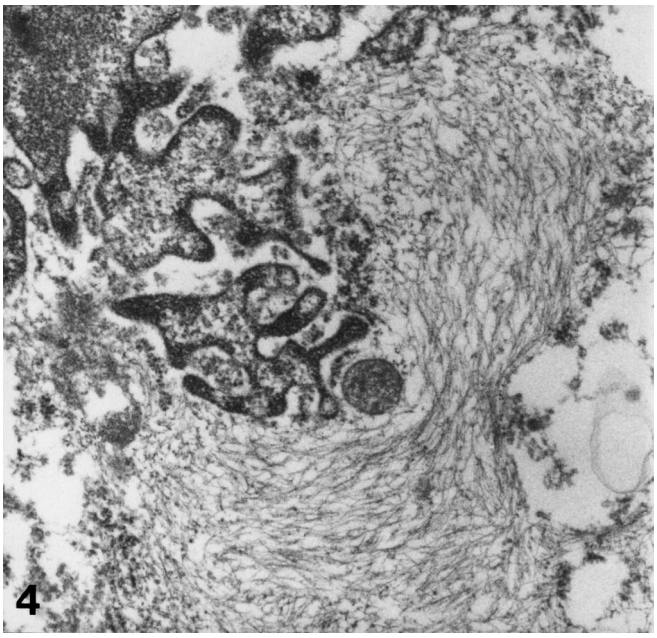

Fig. 4 Case 4. Electron microscopy reveals intracytoplasmic filamentous inclusions. × 14 300

slightly expressed in cases 1 a and 5, and variable positivity for S100 was seen in cases 1 a, 2, 4 and 5. Reactions with antibodies against synaptophysin were negative in all cases.

Immunohistochemical reaction for epithelial antigens was not consistent and when present, only with mild intensity. Cases 1 a, 2 and 5 showed mild expression of EMA. Except for case 4, immunohistochemical stains exhibited variable immunopositivity with antibodies against keratin. In these cases, keratin positivity was restricted to the large tumor cells.

There was a differing reactivity for smooth muscle actin in all tumors (Fig. 2 d); this might be interpreted as a sign of smooth muscle cell characterization, but it is much more likely that actin-positive immunohistochemistry is an unspecific sign of differentiation. However, actin is expressed by a number of tumors of various histogenesis [33]. Desmin was not detectable in any of our cases. Staining with antibodies against GFAP revealed slight expression in four tumors (Fig. 2 c). GFAP-positive cells consisted of large, polygonal cells with abundant cytoplasm. There were only few cells stained with antibodies against AFP in case 5.

Electron microscopy

Electron microscopy revealed similar phenomena in all cases studied. The tumor cells possessed intracytoplasmic fibrillar whorls (Fig. 4). These masses were not connected with membranes and consisted of bundles of approximately 10-nm filaments; they most likely corresponded to the globular inclusions seen on light microscopy. Some of the cell nuclei showed marked indentation by the cytoplasmic aggregates. Occasionally, cellular organelles such as rough endoplasmic reticulum, mitochondria and tubulovesicular structures were displaced by accumulations of the filament bundles or were incorporated into the whorls. There was no evidence of skeletal or smooth muscle differentiation; no myofilaments, sarcomeres or basement membranes were observed.

Discussion

Malignant rhabdoid tumor was originally described by Beckwith and Palmer [4] as a variant of Wilms' tumor of the kidney, "rhabdomyosarcomatoid neoplasm", due to the presence of abundant acidophilic cytoplasm in most tumor cells, often resembling that of skeletal muscle myoblasts but lacking the cytoplasmic striations, ultrastructural features, and immunocytochemical markers of skeletal muscle cells. Haas et al. [19] characterized the tumor as an entity distinct from Wilms' tumor, with typical light microscopic, electron microscopic and immunohistochemical properties. This view was supported by Beckwith [3].

Weeks et al. [48] attempted to distinguish clearly between rhabdoid tumor of the infant kidney and extrarenal rhabdoid tumors, proposing that "childhood rhabdoid tumors of the kidney represent a histogenetic and clinical entity with considerable morphological diversity, and that extrarenal rhabdoid tumors will eventually emerge as a phenotypic concept encompassing a spectrum of histogenetic and clinical diversity".

The association of rhabdoid tumors of the kidney with different embryonal primary tumors originating in the CNS, as noted by Bonnin et al. [6], is quite remarkable. These neuroepithelial tumors included three medulloblastomas, one pineoblastoma, one primitive neuroepithelial tumor, one malignant subependymal giant cell astrocytoma and one cerebellar medulloepithelioma. Bonnin et al. [6] suggested that the coexistence of a rhabdoid tumor of the kidney with a separate primary tumor of the CNS could indicate a neural origin of rhabdoid tumors.

Some authors favor a mesenchymal origin of this tumor due to its occurrence at so many different primary sites [41]. Primary extrarenal rhabdoid tumors have been described at several different sites such as the liver [30], paravertebral region [2, 28], chest wall [18], limbs [25], pelvis [14, 16], heart [40], thoracic spine [35, 43], skin [13], tongue [32], uterus [11], vulva [34], prostate [15], soft tissue [45], urinary bladder [8, 21], inguinal region [46], prepubic region [44], spermatic cord [24] and orbit [36]. Other investigators suggested that MRT of the brain may originate in the leptomeninges. Tumor location with subarachnoid invasion and diffuse meningeal spread of some MRT raise the possibility of a meningothelial cell origin [1, 5, 12, 22, 47].

To define more clearly the histogenesis of cerebral MRT, we studied its immunocytochemical properties. The diagnosis of MRT in the five case reports presented here was based on three criteria: (1) typical light microscopic

morphology with uniformly round tumor cells, vacuolated cytoplasm with occasional round, hyaline intracytoplasmic, PAS-positive inclusions, vesicular nuclei with prominent nuclei; (2) ultrastructural findings of cytoplasmic aggregates of filaments not bounded by membranes and loosely intermingled with normal organelles; and (3) positive immunoreactivity for vimentin.

A skeletal muscle differentiation seems unlikely on the basis of the ultrastructural features, the absence of Z-bands or basal lamina, and negative immunohistochemical staining for myoglobin [9, 10]. Our findings also do not favor a skeletal muscle origin since immunohistochemical staining for desmin was negative. However, we found a variable reaction with antibodies against smooth muscle actin, which was also noted in the CNS-MRT of Chi et al. [10] and in four of the examined five tumors of Parham et al. [31]. An additional two cases of Chou and Anderson [12] and one of Horn et al. [22] presented no staining with antibodies against actin. Desmin was expressed in two of three stained tumors examined by Parham et al. [31]. Other myogenous antigens such as myosin and myoglobin were not found in the tumor samples reported in the literature.

A review of the literature shows that reactivity with vimentin is the most consistent immunohistochemical finding in MRT (20 of 20 examined cases were immunopositive). The aggregated vimentin filaments and rare primitive cell junctions are seen ultrastructurally and immunohistochemically [5, 42]. Ghadially [17] emphasized that vimentin is found in many different cells and may represent a marker of a poorly differentiated phenotype. Our six tumors as well as all of the other cases described in the literature displayed a moderate to marked immunopositivity for vimentin. However, one may speculate whether a cerebral MRT with characteristic light microscopic and ultrastructural features can be diagnosed in the absence of vimentin positivity.

In the literature, 17 of the 19 primary MRT of the brain stained with antibodies against EMA showed different immunohistochemical reactions. The results for another epithelial marker, cytokeratin, which was variably expressed in 12 of 17 examined tumors, were similar. Of our 6 investigated MRT 3 stained positive with EMA and 5 of 6 expressed cytokeratin (Table 1).

Expression of GFAP was found in only 6 of 15 MRT in the literature. Agranovich et al. [1], Hanna et al. [20] and Weeks et al. [49] found a moderate immunopositivity for GFAP, Molenaar [29] found a strong expression. GFAP was expressed mildly in 4 of our 6 tumors. Immunopositivity for S100 was exhibited in 7 of 11 neoplasms (Table 2). Of our 6 examined tumors 4 expressed weak to moderate S100 immunopositivity.

Only one of our tumors expressed AFP mildly, in contrast to the two MRT examined by Chou and Anderson [12], which were immunonegative for AFP. The differential diagnosis of a germ cell tumor or an embryonal carcinoma was excluded by the differing histological morphology and the immunonegativity with antibodies against human choriongonadotropin and placenta-alkalic phosphatase in our tumors. In addition we would have to expect our examined brain tumors to be metastases from primary germ cell tumors or embryonal carcinomas, which, however, has been reliably excluded by various radiological and serological examinations.

The neural antigen expression pattern has only occasionally been studied in the literature. Pan-NF expression was investigated in only 6 MRT; all but 1 were negative [5, 33, 47]. NF subtypes were not detected in one cerebral rhabdoid tumor studied by Molenaar et al. [29]. We examined our cases with NF antibodies against the different intermediate filaments of 68-, 160- and 200-kDa molecular mass and found them to be immunopositive. The specifity of the immunoreaction was confirmed in other neuronal tumors such as gangliogliomas, whereas glial tumors such as ependymoma or glioblastoma were consistently negative. NSE was expressed in 2 of our 6 tumors. In the literature 9 positive immunohistochemical reactions for NSE were described [20, 49]. Using antibodies against synaptophysin Perilongo et al. [33] and Horn et al. [22] failed to show a neural component of MRT. Our tumors did not express synaptophysin. This constant or partial immunonegativity for the neural markers synaptophysin and NSE in our tumors does not exclude the hypothesis of a neuroectodermal origin of extrarenal rhabdoid tumors. Kleinert [27] investigated 35 different primitive neuroectodermal tumors with various neuronal markers, of which 17 were medulloblastomas, as an example for a poorly differentiated neuronal tumor. He found that 6 of 17 tumors were negative for each of the neuronal markers synaptophysin and NSE. Thus, a negative NSE or synaptophysin reactin does not seem to exclude a tumor of neural origin. Synaptophysin is claimed to be a neuronal marker for well-differentiated, mature neurons. Our tumors might just be too poorly differentiated to reveal synaptophysin reaction. Kleinert [26] also states that different neurofilament markers, which may also reveal stages of the neuroectodermal differentiation, are expressed in poorly differentiated as well as in mature neurons. Also, since it is still controversial which NF subtype is expressed at which stage of differentiation, the different subtypes in our tumors might indicate tumors of poorer differentiation than synaptophysin, as a marker for mature neurons, is able to stain.

Rorke et al. [37] recently collected 32 CNS tumors designated as atypical teratoid/rhabdoid tumors of infancy and childhood; the patients' ages ranged from 1 month to 12 years. The different microscopical patterns and immunohistochemical profiles in these tumors were studied (see Table 2). Rhabdoid cells were seen in all tumors and two-thirds contained "primative neuroectodermal tumor-like cells". A mesenchymal and epithelial component could be observed in only a few of the tumors. As described above, different tumor cell populations were also seen in our cases. Rorke et al. [37] found a striking immunopositivity for EMA in 93% as opposed to only 50% in our cases. In comparison to our findings they showed similar results as to the high expression for vimentin and smooth muscle actin. However, only 24% of their atypical tera-

Table 2 Immunohistochemical findings of primary malignant rhabdoid tumors of the central nervous system reported by various authors. Values and abbreviations as in Table 1 (*1-a-Chy* α-1-anti-chymotrypsin, *B1* B lymphocytes, *CEA* carcino-embryonic antigen, *CLA* common leucocyte antigen, *CROM A* chromagranin A, *HAM 56* muramidase (macrophage), *CKK* cytokeratin, *Leu-7* leucocytes, *Lysoz* lysozyme, *Myogl* Myoglobin, *nd* not determined)

	VIM	NF	NSE	SYN	GFAP	Actin	Des-min	Myo-sin	MYO GL	EMA	CK	S-100	AFP	CEA	CLA	Leu-7	B1	HAM 56	Chrom A	Lys-oz	1-a-Chy
Briner et al. [7]	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	X	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
Biggs et al. [5]	X	0	nd	nd	0	nd	0	0	0	0	0	0	nd	nd	nd	nd	nd	nd	nd	nd	nd
Jakate et al. [23]	X	nd	0	nd	nd	nd	0	nd	nd	X	X	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
Chi et al. [10]	XXX	nd	0	nd	0	X	nd	nd	0	X	XXX	0	nd	nd	nd	nd	nd	nd	0	nd	nd
Molenaar et al. [29]	XXX	0	nd	nd	XXX	nd	nd	nd	nd	XXX	XXX	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
Perilongo et al. [33]	X	0	nd	0	0	nd	0	nd	nd	XXX	0	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
Chou & Anderson [12]	X	nd	0	nd	0	0	0	nd	0	X	0	nd	0	0	nd	nd	nd	nd	nd	nd	nd
	XX	nd	0	nd	0	0	0	nd	0	XX	X	nd	0	0	0		0	0			
Agranovich et al. [1]	X	nd	X	nd	X	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
Horn et al. [22]	X	nd	0	0	0	0	0	0	0	X	0	0	nd	0	0	nd	0	nd	nd	nd	0
Velasco et al. [47]	X	0	0	nd	0	nd	0	nd	0	0	0	0	nd	nd	nd	nd	nd	nd	0	0	0
Hanna et al. [20]	XXX	nd	XX	nd	0	nd	nd	nd	nd	XX	XX	XXX	nd	nd	nd	0	nd	nd	nd	nd	nd
	XXX	nd	0	nd	0	nd	nd	nd	nd	XXX	XXX	XX	nd	nd	nd	XXX	nd	nd	nd	nd	nd
	XX	nd	X	nd	XX	nd	nd	nd	nd	XX	X	XXX	nd	nd	nd	0	nd	nd	nd	nd	nd
Satoh et al. [38]	X	0					0	0		X	X										
Parham et al. [31]	XX				XXX	XXX				X											
	XXX		X			XX				X	XX	XX				X					
	XXX					0				XX	X					X					
	XXX	X	XX			X	0			XX		X				X					
			XXX				X														
			XXX																		
	XXX		XXX		X	X	X			XX	X	XXX				X					
Weeks et al. [49]	XX	nd	XX	nd	XX	nd	nd	nd	nd	XX	nd	XX	nd	nd	nd	nd	nd	nd	nd	nd	nd
Rorke et al. [37]	XXX	XX	nd	XX	XXX	XXX	XX	nd	nd	XXX	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd

toid/rhabdoid tumors examined revealed an immunopositivity for NF, in contrast to the striking expression of different neurofilaments in all of our cases. This would support the hypothesis of a close relationship to neural tumors.

Weeks et al. [49] described a primitive cerebral tumor in a 26 month-old boy exhibiting phenotypic rhabdoid features suggestive of neuroglial derivation. The tumor expressed S100, NSE and GFAP besides vimentin and EMA. Immunohistochemistry with antibodies against NF was not performed. The interpretation of their data was that they had identified features of primitive neuroglial differentiation not seen in renal MRT. This further suggested that primary MRT of the brain likely represents a distinctive type of neuroglial neoplasm more closely related to other primitive brain tumors than to MRT of the kidney.

The expression of NF of 68, 160 and 200 kDa in our cases of cerebral MRT was prominent and has to be confirmed in further studies since similar findings have not been described in the literature. This remarkable positivity of neural differentiation in all of our cases is supported by the finding that one of the MRT investigated expressed NCAM, an early marker of neural differentiation. However, NCAM may be expressed in a variety of non-neural tumors such as lymphomas or in non-neural cells such as those of the thyroid. Therefore, NCAM positivity suggests, but cannot prove, neural differentiation in these tumors.

References

1. Agranovich AL, Ang LC, Griebel RW, Kobrinsky NL, Lowry N, Tchang SP (1992) Malignant rhabdoid tumor of the central nervous system with subarachnoid dissemination. Surg Neurol 37:410–414
2. Balaton AJ, Vaury P, Videgrain M (1987) Paravertebral malignant rhabdoid tumor in adult: a case report with immunocytochemical study. Pathol Res Pract 182:713–718
3. Beckwith JB (1983) Wilms' tumor and other renal tumors of childhood: a selective review from the National Wilms' Tumor Study Pathology Center. Hum Pathol 14:481–492
4. Beckwith JB, Palmer NF (1978) Histopathology and prognosis of Wilms' tumor. Results from the First National Wilms' Tumor Study. Cancer 41:1937–1948
5. Biggs PJ, Garen PD, Powers JM, Garvin AJ (1987) Malignant rhabdoid tumor of the central nervous system. Hum Pathol 18:332–337
6. Bonnin JM, Rubinstein LJ, Palmer NF, Beckwith JB (1984) The association of embryonal tumors originating in the kidney and in the brain. Cancer 54:2137–2146
7. Briner J, Bannwart F, Kleihues P, Odermatt B, Janzer R, Willi U (1985) Malignant small cell tumor of the brain with intermediate filaments. A case of primary cerebral rhabdoid tumor (abstract). Pediatr Pathol 3:117–118
8. Carter RL, McCarthy KP, Al-Sam SZ, Monagham P, Agrawal M, McElwain TJ (1989) Malignant rhabdoid tumor of the bladder with immunohistochemical and ultrastructural evidence suggesting histiocytic origin. Histopathology 14:179–190
9. Chang C-H, Ramirez N, Sakr WA (1989) Primitive neuroectodermal tumor of the brain associated with malignant rhabdoid tumor of the liver; a histologic, immunohistochemical, and electron microscopic study. Pediatr Pathol 3:307–319
10. Chi Y-W, Lee W-H, Hwang R-C, Liao H-B, Cheng S-N, Chu M-L, Chou T-Y, Ho PSP (1989) Intracranial malignant rhabdoid tumor: report of one case. Acta Paediatr Sin 30:316–322
11. Cho KR, Rosenhein NB, Epstein JI (1989) Malignant rhabdoid tumor of the uterus. Int J Gynecol Pathol 8:381–387
12. Chou SM, Anderson JS (1991) Review: primary CNS malignant rhabdoid tumor (MRT): report of two cases and review of literature. Clin Neuropathol 10:1–10
13. Dabbs DJ, Park HK (1988) Malignant rhabdoid skin tumor: an uncommon primary skin neoplasm, ultrastructural and immunohistochemical analysis. J Cutan Pathol 15:109–115
14. Dervan PA, Cahalane SF, Kneafsey P, Mynes A, McCallister K (1987) Malignant rhabdoid tumor of soft tissue: an ultrastructural and immunohistological study of a pelvic tumor. Histopathology 11:183–190
15. Ekfors TO, Aho HJ, Kekomäki M (1985) Malignant rhabdoid tumor of the prostatic region: immunohistological and ultrastructural evidence of epithelial origin. Virchows Arch [A] 406:381–388
16. Frierson HF Jr, Mills SE, Innes DJ Jr (1985) Malignant rhabdoid tumor of the pelvis. Cancer 55:1963–1967
17. Ghadially FN (1985) Diagnostic electron microscopy of tumors, 2nd edn. Butterworths, London, pp 344–361
18. Gonzalez-Crussi F, Goldschmidt RA, Hsueh W, Trujillo YP (1982) Infantile sarcoma with intracytoplasmic filamentous inclusions. Cancer 1982;49:2365–2375
19. Haas JE, Palmer NF, Beckwith JB (1981) Ultrastructure of malignant rhabdoid tumor of the kidney. Hum Pathol 12:646–657
20. Hanna SL, Langston JW, Parham DM, Douglass EC (1993) Primary malignant rhabdoid tumor of the brain: clinical, imaging, and pathologic findings. AJNR 14:107–115
21. Harris M, Eyden BP, Joglekar VM (1987) Rhabdoid tumor of the bladder: a histological, ultrastructural and immunohistochemical study. Histopathology 11:1083–1092
22. Horn M, Schlote W, Lerch KD, Steudel WI, Thomas E (1992) Malignant rhabdoid tumor: primary intracranial manifestation in an adult. Acta Neuropathol 83:445–448
23. Jakate SM, Marsden HB, Ingram L (1988) Case report: primary rhabdoid tumour of the brain. Virchows Arch [A] 412:393–397
24. Kawanishi Y, Tamura M, Akiyama K, Akiyama M, Tanaka T, Numata A, Yuasa M, Imagawa A (1989) Rhabdoid tumor of the spermatic cord. Br J Urol 53:439–440
25. Kent AL, Mahoney DH Jr, Gresik MV, Steuber CP, Fernbach DJ (1987) Malignant rhabdoid tumor of the extremity. Cancer 60:1056–1059
26. Kleinert R (1991) Immunohistochemical characterization of primitive neuroectodermal tumors and their possible relationship to the stepwise ontogenetic development of the central nervous system. 1. Ontogenetic studies. Acta Neuropathol 82:502–507
27. Kleinert R (1991) Immunohistochemical characterization of primitive neuroectodermal tumors and their possible relationship to the stepwise ontogenetic development of the central nervous system. 2. Tumor studies. Acta Neuropathol 82:508–515
28. Lynch HT, Shurin SB, Dahms BB, Izant RJ, Lynch J, Danes BS (1983) Paravertebral malignant rhabdoid tumor in infancy, in vitro studies of a familial tumor. Cancer 52:290–296
29. Molenaar WM, Jansson DS, Gould VE, Rorke LB, Franke WW, Lee VM-Y, Packer RJ, Trojanowski JQ (1989) Molecular markers of primitive neuroectodermal tumors and other pediatric central nervous system tumors. Lab Invest 61:635–643
30. Parham DM, Peiper SC, Robicheaux G, Ribeiro RC, Douglass EC (1988) Malignant rhabdoid tumor of the liver: evidence for epithelial differentiation. Arch Pathol Lab Med 112:61–64
31. Parham DM, Weeks DA, Beckwith JW (1994) The clinicopathologic spectrum of putative extrarenal rhabdoid tumors. An analysis of 42 cases studied with immunohistochemistry of electron microscopy. Am J Surg Pathol 18:1010–1029

32. Patron M, Palacios J, Rodriguez-Peralto JL, Burgo E, Contreras F (1988) Malignant rhabdoid tumor of the tongue: a case report with immunohistochemical and ultrastructural findings. Oral Surg Oral Med Oral Pathol 65 : 67–70
33. Perilongo G, Sutton L, Czaykowski D, Gusnard D, Biegel J (1991) Rhabdoid tumor of the central nervous system Med Pediatr Oncol 19 : 310–317
34. Perrone T, Swanson PE, Twiggs L, Ulbright TM, Dehner LP (1989) Malignant rhabdoid tumor of the vulva: is distinction from epitheloid sarcoma possible? A pathologic and immunohistochemical study. Am J Surg Pathol 13 : 848–858
35. Robson DB, Akbarnia BA, Connors RH, Crafts DC (1987) Malignant rhabdoid tumor of the thoracic spine. Spine 12 : 620–624
36. Rootman J, Damji KF, Dimmick JE (1989) Malignant rhabdoid tumor of the orbit. Ophthalmology 96 : 1650–1654
37. Rorke LB, Packer R, Biegel J (1995) Central nervous system atypical teratoid/rhabdoid tumors of infancy and childhood. J Neurooncol 24 : 21–28
38. Satoh H, Goishi J, Sogabe T, Uozumi T, Kiya K, Migita K (1993) Primary malignant rhabdoid tumor of the central nervous system: case report and review of the literature. Surg Neurol 40 : 429–434
39. Skalli O, Roptraz P, Trzeciak A, Benozonana G, Gillessen D, Gabbiani G (1986) A monoclonal antibody against alpha-smooth muscle actin: a new probe for smooth muscle differentiation. J Cell Biol 103 : 2787–2796
40. Small EJ, Gordon GJ, Dahms BB (1985) Malignant rhabdoid tumor of the heart in an infant. Cancer 55 : 2850–2853
41. Sotelo-Avila C, Gonzalez-Crussi F, deMello D, Vogler C, Gooch WM, Gale G, Pena R (1986) Renal and extrarenal rhabdoid tumors in children: a clinicopathologic study of 14 patients. Semin Diagn Pathol 3 : 151–163
42. Takagi M, Takakuwa T, Ushigoma S, Nakata K, Fugiloka T, Watanabe A (1987) Sarcomatous variants of Wilms' tumor. Cancer 59 : 963–971
43. Tantana S, Sotelo-Avila C, Pilla TJ, Sundaram M (1988) Malignant rhabdoid tumor of the thoracic spine. Orthopedics 11 : 905–908
44. Tsujimura T, Wada A, Kawano K, Iwasa A, Mizutani S (1989) A case of malignant rhabdoid tumor arising from soft parts in the prepubic region. Acta Pathol Jpn 39 : 677–682
45. Tsuneyoshi M, Daimaru Y, Hashimoto H, Enjoji M (1985) Malignant soft tissue neoplasms with the histologic features of renal rhabdoid tumors: an ultrastructural and immunohistochemical study. Hum Pathol 16 : 1235–1242
46. Uchida H, Yokoyama S, Nakayama I, Zeze K (1988) An autopsy case of malignant rhabdoid tumor arising from soft parts in the left inguinal region. Acta Pathol Jpn 38 : 1087–1096
47. Velasco ME, Brown JA, Kini J, Ruppert ES (1993) Primary congenital rhabdoid tumor of the brain with neoplastic hydranencephaly. Child Nerv Syst 9 : 185–190
48. Weeks DA, Beckwith JB, Mierau GW (1989) Rhabdoid tumor. An entity or a phenotype? Arch Pathol Lab Med 113 : 113–114
49. Weeks DA, Malott RL, Zuppan CW, Liwnicz BH, Beckwith JB (1994) Primitive cerebral tumor with rhabdoid features: a case of phenotypic rhabdoid tumor of the central nervous system. Ultrastr Pathol 18 : 23–28