Virchows Archiv A Pathol Anat (1993) 422:81–85

Virchows Archiv A
Pathological Anatomy and Histopathology

Case report

Rhabdoid tumours of the central nervous system

Report of three cases with immunocytochemical and ultrastructural findings

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Received March 11, 1992 / Received after revision June 11, 1992 / Accepted June 15, 1992

Summary. Three cases of rhabdoid tumour of the central nervous system arising in a supratentorial location are reported. The patients were 18, 14, and 7 years old. All three tumours showed a common morphology. The neoplastic cells were usually globoid with round nuclei and prominent nucleoli and large acidophilic, cytoplasmic inclusions were present in many of them. These inclusions showed strong immunoreactivity for vimentin, weak immunoreactivity for epithelial membrane antigen and focal immunoreactivity for cytokeratins. Ultrastructurally they were made up of whorls of intermediate filaments, 8–10 nm in thickness. Rhabdoid tumours of the central nervous system, whatever the cell of origin, appear to be an independent entity with identifiable histology and aggressive behaviour.

Key words: Rhabdoid tumour – Central nervous system – Immunocytochemistry – Ultrastructure

Introduction

Rhabdoid tumour (RT) is an aggressive malignant neoplasm originally described in the kidney by Beckwith and Palmer (1978) as a variant of Wilms' tumour. Subsequently RT has been identified as a distinct clinicopathological entity, occurring mostly in children (Haas et al. 1981).

Since the first description, primary RTs have been reported in a variety of extrarenal locations, such as the thymus (Lemos and Hamoudi 1978), liver (Gonzales-Crussi et al. 1982; Parham et al. 1988), soft tissues (Kent et al. 1987; Kodet et al. 1991; Sotelo-Avila et al. 1986), heart (Small et al. 1985), urinary bladder (Harris et al. 1987), paravertebral region (Balaton et al. 1987; Lynch et al. 1983), pelvis (Dervan et al. 1987; Frierson et al. 1985), prostate (Ekfors et al. 1985), vulva (Perrone et al. 1989) and uterus (Cattani et al. 1992). Only six cases of primary RT have been reported in the central nervous system (CNS), three of them occurring in the cerebellum (Biggs et al. 1987; Jakate et al. 1988; Kapur et al. 1986), one in the parietal lobe (Briner et al. 1985), one in the temporal lobe (Sotelo-Avila et al. 1986) and one in the posterior fossa (Biegel et al. 1990).

We have recently observed three cases of RT of the CNS, all of them presenting in a supratentorial location. Their clinicopathological and immunohistochemical features are the subject of this report.

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Case reports

Case 1

The patient was a previously healthy 18-year-old man hospitalized in a department of neurosurgery because of persistent headache. Clinical examination revealed papilloedema and raised intracranial pressure. A CT scan showed a large mass in the left frontal lobe. At surgery a greyish tumour was removed, 7 cm in diameter and easily separable from the adjacent brain. A histological diagnosis of RT was made. Postoperatively, the patient received two courses of chemotherapy. Five months later, the tumour recurred and required a further surgical resection. No additional therapy was given. Eleven months later another local recurrence was detected which was judged inoperable. The patient died shortly thereafter.

Case 2

A 14-year-old girl presented with symptoms of raised intracranial pressure. A CT scan revealed a large intracerebral tumour in the temporo-occipital region of the right hemisphere (Fig. 1). At surgery the tumour was only removed partially and a diagnosis of fibrillary astrocytoma was made. Seven months later the tumour

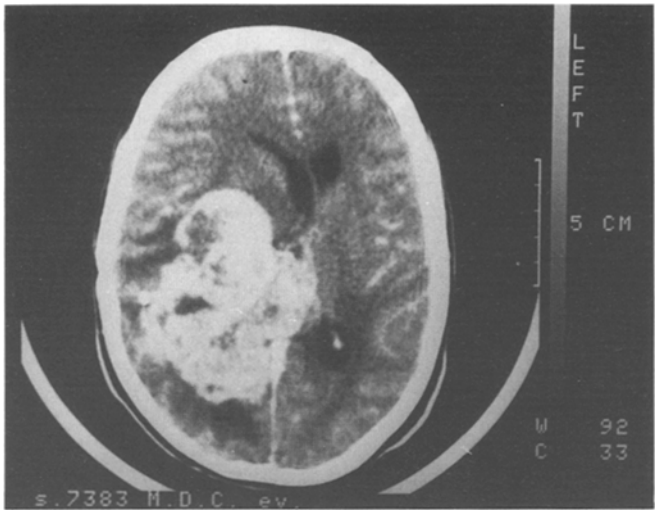

Fig. 1. CT scan of the brain showing a large mass in the right temporo-occipital region. The neoplasm displaces the ventricular system. Case 2

recurred and the patient underwent a second operation. At this point a diagnosis of RT was made and a course of radiotherapy (60 Gy) was administered. The patient had a second local relapse of the neoplasm 6 months later and underwent further surgery. She died 25 months after the first operation.

Case 3

A 7-year-old boy was admitted to hospital because of vomiting, aphasia and right hemiparesis. CT scan and magnetic resonance imaging showed a subcortical tumour in the left parietal lobe. At craniotomy a large neoplasm was found and only excised partially. After the diagnosis of RT the patient was given five courses of chemotherapy and a course of radiotherapy. He is alive 25 months after surgery.

Materials and methods

From all cases, formalin-fixed tissue was routinely processed and stained with haematoxylin and eosin and the periodic acid-Schiff (PAS) method following diastase digestion.

Immunostaining was carried out by the avidin-biotin-peroxidase complex method (Hsu et al. 1981). Paraffin-embedded sections (4 μm) were incubated with monoclonal antibodies to vimentin (Dakopatts, Glostrup, Denmark), desmin (Dakopatts), alpha-sarcomeric actin (Sigma, St. Louis, Mo., USA) alpha-smooth-muscle actin (Sigma), muscle actin (Enzo, New York, USA), cytokeratins A (Enzo), B (Enzo), AE1 (Signet, Dedham, Mass., USA), AE3 (Signet) and CAM 5.2 (Becton-Dickinson, Mountain View, Calif., USA). The following polyclonal antisera were also used: anti-myoglobin (Dakopatts), anti-glial fibrillary acidic protein (GFAP) (Dakopatts), anti-S100 protein (Dakopatts), anti-neuron specific enolase (NSE) (Dako, Santa Barbara, Calif., USA), anti-epithelial membrane antigen (EMA) (DPC, Los Angeles, Calif., USA) and anti-neurofilaments (Sclavo, Siena, Italy). Adequate positive and negative controls were used.

For ultrastructural examination formalin-fixed tissues from cases 1 and 3 were post-fixed in osmium tetroxide and embedded in Durcupan resin. Ultrathin sections were stained with uranyl acetate and lead citrate and examined under an electron microscope (Zeiss EM 109).

Results

All cases showed very similar morphological findings and are described together.

Microscopic examination showed a proliferation of medium to large-sized cells, growing in a diffuse pattern. The neoplastic cells had an oval or polygonal shape with abundant, eosinophilic cytoplasm showing occasional "ground-glass" appearance. Nuclei were round with prominent, usually single, centrally placed nucleoli. The nuclei were often characteristically displaced to the periphery of the cells by a large cytoplasmic inclusion of amorphous PAS-positive material (Fig. 2). Numerous

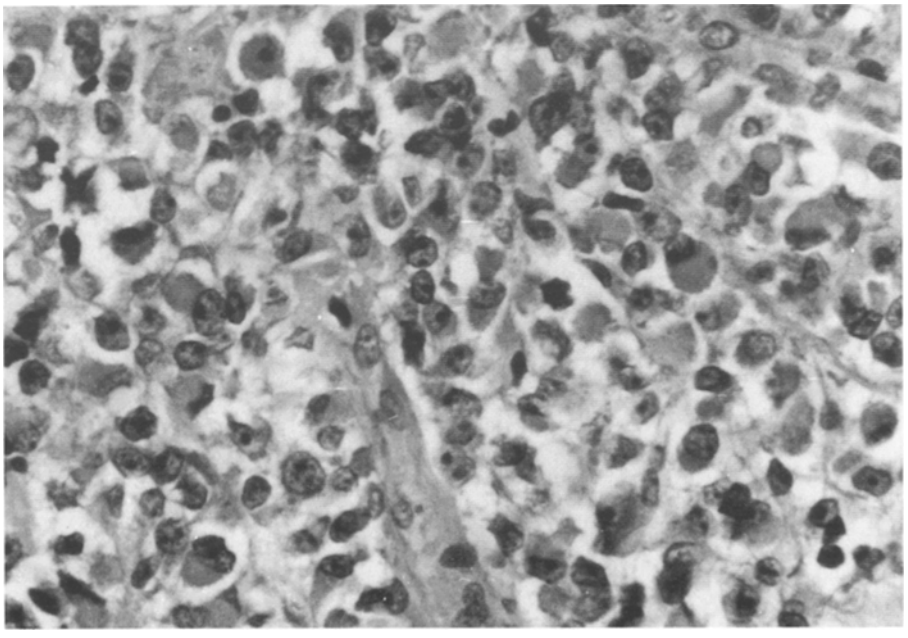

Fig. 2. In light microscopy many neoplastic cells with typical abundant eosinophilic cytoplasm and eccentric nuclei are clearly recognizable. Case 3. ×600

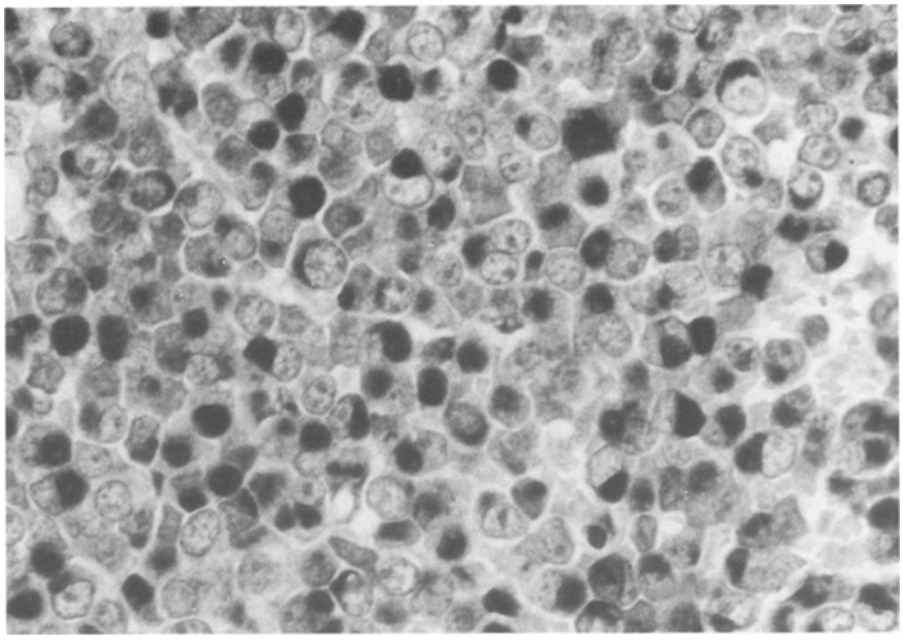

Fig. 3. Immunohistochemical reactivity for vimentin in cerebral rhabdoid tumour. The cytoplasmic inclusions are strongly immunostained. Note also the prominent nucleolus located in a central position. Case 1. ×680

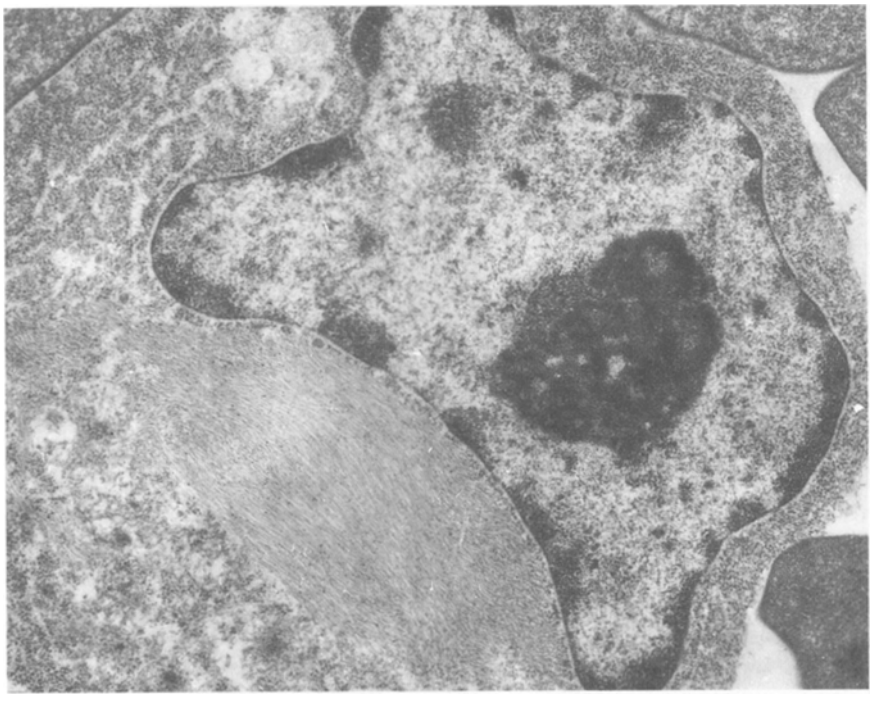

Fig. 4. Electron microscopy shows the paranuclear inclusions to be made up of bundles of intermediate filaments, 8–10 nm. Case 1. ×14500

neoplastic cells with empty cytoplasmic vacuoles were noted in case 2. Numerous mitoses were seen in all cases.

All neoplastic cells displayed strong immunoreactivity for vimentin (Fig. 3), which most often appeared to be condensed in large, globoid inclusions adjacent to and sometimes obscuring the nucleus. Occasional cells were also immunoreactive for EMA, showing both a granular cytoplasmic positivity and a strong decoration of the cell membranes. The anti-NSE antibody gave a weak cytoplasmic staining in all cases. Scattered tumour cells of case 1 reacted for cytokeratins, using the CAM 5.2, cytokeratin A and AE3 mAbs. In case 2 occasional cells reacted with the anti-GFAP antiserum. Neoplastic cells immunoreactive for the remaining antibodies were not observed in any of the three cases.

Ultrastructural examination showed the neoplastic cells to be large and polyhedral in shape. Nuclei were usually round and contained a single, prominent nucleolus and dispersed chromatin. There was no nuclear pleomorphism but occasionally nuclear folding and lobulations were observed. The most striking feature was the presence in the cytoplasm of abundant intermediate filaments, 8–10 nm in thickness, which tended to displace the cytoplasmic organelles peripherally (Fig. 4). The fila-

Table 1. Clinical features of primary rhabdoid tumours of central nervous system

	Age at diagnosis	Sex	Site	Follow-up
Briner et al. (1985)	3 months	M	Left parietal lobe	Died after 2.5 months
Sotelo-Avila et al. (1986)	13 years	M	Left temporal lobe	Died after 3 months
Biegel et al. (1990)	1 year	F	Posterior fossa	Died after 5 months
Kapur et al. (1986)	5 years	M	Cerebellum	Not known
Biggs et al. (1987)	3 months	M	Cerebellum	Died after 2 weeks
Jakate et al. (1986)	3 years	M	Cerebellum	Alive after 5 months
Case 1	18 years	M	Left frontal lobe	Died after 1.5 years
Case 2	14 years	F	Right temporo-occipital region	Died after 25 months
Case 3	7 years	M	Left parietal lobe	Alive after 25 months

ments always had a paranuclear location and were arranged in bundles with concentric whorls.

Discussion

The pathological features of the three cases presented in this report are similar to those previously described in RTs (Haas et al. 1981; Sotelo-Avila et al. 1986; Weeks et al. 1989a). All neoplasms were formed of a monotonous proliferation of cells with the typical cytoplasmic aggregates of filaments and roundish nuclei showing prominent nucleoli. Paranuclear bodies made up of thin filaments have also been described in RT at the ultrastructural level (Haas et al. 1981; Sotelo-Avila et al. 1986; Weeks et al. 1989a).

Most of the neoplastic elements of our cases were strongly and diffusely positive with vimentin antiserum, focally positive for EMA and cytokeratins and are consistent with previous reports of RT (Kodet et al. 1991).

Moreover, careful clinical investigations failed to reveal any possible primary tumour located elsewhere in the body and the neoplasms were considered to be primary in the CNS.

Of the six cases hitherto published of primary RT of CNS three occurred in the cerebellum, respectively in 3-month, 3- and 5-year-old children (Briner et al. 1985; Jakate et al. 1988; Kapur et al. 1986); three were reported in a supratentorial location in 1-year, 3-month and 13-year-old patients (Biegel et al. 1990; Biggs et al. 1987; Sotelo-Avila et al. 1986). All three cases reported here were located in supratentorial sites and, in two cases, in older patients. Our clinical data are in agreement with previous studies of RTs of the brain and confirm the aggressive behaviour of these neoplasms.

Primary tumours with rhabdoid features have been reported in extrarenal locations (Balaton et al. 1987; Cattani et al. 1992; Dervan et al. 1987; Ekfors et al. 1985; Frierson et al. 1985; Gonzalez-Crussi et al. 1982; Harris et al. 1987; Kent et al. 1987; Kodet et al. 1991; Lemos and Hamoudi 1978; Lynch et al. 1983; Parham et al. 1988; Perrone et al. 1989; Small et al. 1985; Sotelo-Avila et al. 1986; Tsuneyoshi et al. 1986) but some disagreement has arisen over the interpretation of these neoplasms as true RTs. Weeks et al. (1989b), in an interesting editorial, pointed out that extrarenal RTs "emerge as a phenotypic concept encompassing a spectrum of histogenetic and clinical diversity". Also, Tsuneyoshi and colleagues (1986) were able to demonstrate the presence of cells with typical rhabdoid appearance in a large series of different soft tissue sarcomas. The significance of these findings is not clear, particularly because of the limited number of extrarenal RTs in the literature, but they suggest that many neoplasms are capable of differentiating in a rhabdoid fashion. Moreover, this type of differentiation may lead to a more aggressive clinical outcome.

The cellular origin of RT is disputed; neuroectodermal (Haas et al. 1981), histiocytic (Lemos and Hamoudi 1978), mesenchymal (Sotelo-Avila et al. 1986), and epithelial cells (Higa et al. 1984) have all been suggested but neither immunohistochemical nor ultrastructural studies have elucidated a normal counterpart of RT cells with any certainty. Biggs et al. (1987) discussed the histogenesis of the RT of CNS but did not reach a conclusion. They suggest that the tumour could have a mesenchymal origin although the immunohistochemical demonstration of vimentin is not exclusive to mesenchymal cells; it may indicate cellular immaturity.

A karyotypic anomaly (monosomy 22) was recently described as the only chromosomal change occurring in two rhabdoid tumours of the brain (one of them associated with RT of the left kidney) (Biegel et al. 1990). Evidence for a constant chromosomal alteration would support the hypothesis that extrarenal RTs represent a primitive neoplasm and not an aggressive phenotype.

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