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Case report

Malignant rhabdoid tumor of the prostatic region

Immunohistological and ultrastructural evidence for epithelial origin

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Summary. We describe a malignant rhabdoid tumour of the prostatic region in a 14-year old boy. The tumour showed positive immunoreactivity for epidermal prekeratin, monoclonal cytokeratin, epithelial membrane antigen, carcinoembryonic antigen and monoclonal vimentin but was negative for myoglobin, alfa-fetoprotein and lysozyme. Electron microscopy revealed pleomorphic cells with collections of paranuclear intermediate filaments, sheaves of tonofilaments and abundant microvilli in some tumour cells. Epithelial derivation was also suggested by occasional intracytoplasmic lumina and rare cell junctions.

Key words: Malignant rhabdoid tumor – Intermediate filaments – Ultrastructure

Haas et al. (1981), based on the previous investigations of Beckwith and Palmer (1978) and Palmer et al. (1978), described an unusual and highly malignant renal tumour, which they called malignant rhabdoid tumour, because of its resemblance to rhabdomyosarcoma in light microscopy. Ultrastructural studies, however, have failed to demonstrate any signs of rhabdomyoblastic differentation (Haas et al. 1981; Fung et al. 1981; Schmidt et al. 1982; Rousseau-Merck et al. 1983). The ultrastructural features are compatible with epithelial differentiation (Haas et al. 1981; Higa et al. 1984) and this suggestion is supported by the immunohistological absence of myoglobin (Rutledge et al. 1983) and by the presence of cytokeratin (Vogel et al. 1984; Higa et al. 1984) and epithelial membrane antigen (Higa et al. 1984). The malignant rhabdoid tumour does not seem to confine itself to the kidney, since similar neoplasms have been reported in the liver, chest wall (Gonzales-Crussi et al. 1982) and thymus (Lemos and Hamoudi 1978). Both of these reports suggested a histiocytic origin for the tumour because of

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the phagocytic activity and lysozyme-content of the tumour cells, respectively.

History

The patient was a boy, aged 14 years, who was admitted because of bilateral femoral pains. His previous clinical history was uneventful except for perforated appendicitis, which had been operated less than a month before admission. On clinical examination a firm tumour about 4 cm in diameter was found in retrovesical area. The innervation of the lower extremities was intact. At cystoscopy, the trigone and the posterior wall of prostatic urethra were infiltrated by a soft apparently neoplastic mass. The covering mucosa was heavily folded. In bimanual examination the tumour extended upwards behind the bladder. Chest x-ray was normal, as were the routine blood analyses and bone marrow smear. Specifically, hypercalcaemia was never recorded and the serum level of alphafetoprotein and the daily excretion of methoxymandelic acid were normal.

CAT-scan of the pelvis showed a partially intravesical tumour, which also seemed to thicken the bladder wall. On lymphography, the intrapelvic lymph node chains were seen to be displaced laterally and many nodes showed defects. A few abnormal nodes were noted in the left supraclavicular area.

Since a poorly differentiated pelvic rhabdomyosarcoma was suspected primarily on the basis of clinical history and tumour biopsy, combined chemotherapy with vincristine, actinomycin-D and cyclophosphamide was commenced. As judged by repeated bimanual examination, the clinical response was equivocal. X-ray irradiation was attempted to control the intensive radicular pains. Within weeks, however, this regimen failed. Subradical debulking surgery (Fig. 1) and urinary diversion was undertaken to achieve symptomatic relief. Three weeks after the operation and five months after the first symptoms the patient died with massive pulmonary thromboembolism. At autopsy widespread tumour metastases were found in paraaortal and mediastinal lymph nodes, peritoneum, pleura, lungs and heart.

Material and methods

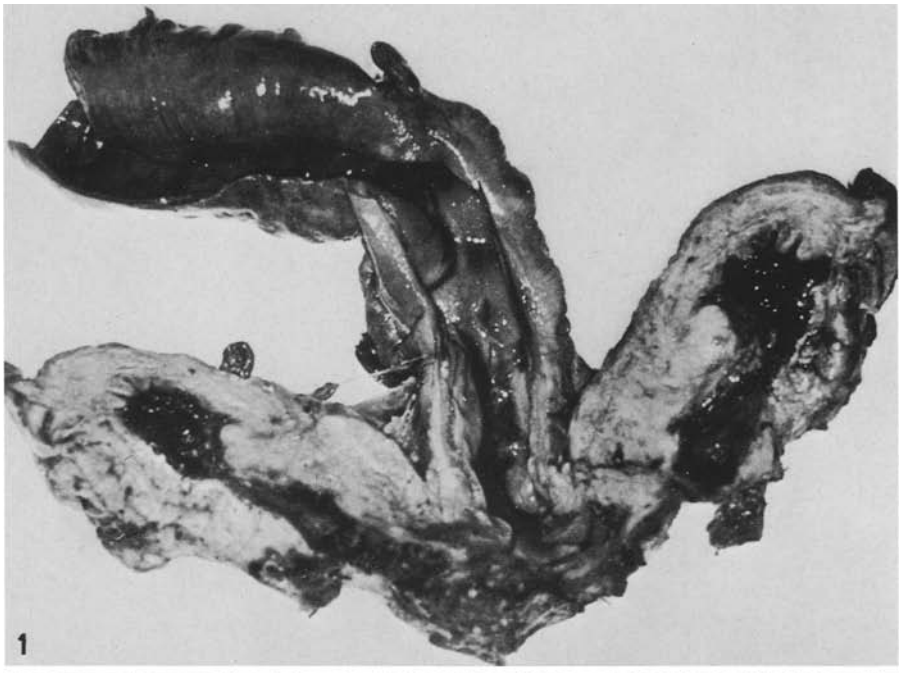
The tumour tissue was sampled from the operative preparation for light and electron microscopy. The stainings of paraffin sections included van Gieson stain, haematoxylin and eosin, PAS with and without diastase pre-treatment, Alcian blue, Grimelius stain for argyrophilia and Gomori stain for reticulin.

Immunohistological stainings were carried out either by using peroxidase-antiperoxidase method for polyclonal antibodies or biotinavidin system (Vectastain®, Vector Laboratories, Burlingame, USA) for monoclonal antibodies. The sources of antibodies were as follows: monoclonal anticytokeratin (PKK1) and monoclonal antivimentin were from Labsystems Co, Helsinki, Finland, epidermal antiprekeratin from Biomeda Corp., Foster City, USA, antiepithelial membrane antigen was a gift from Professor L.C. Andersson, Department of Pathology, University of Helsinki, Finland. Anticarcinoembryonic antigen, antilysozyme and antialfafetoprotein were from Dako-Immunoglobulins A/S (Denmark) and antimyoglobin from Immunolab Inc., Carpinteria, USA. Antibodies were tested with tissues known to contain respective antigens. Negative controls were accomplished by replacing the primary antiserum with normal serum at corresponding dilutions.

The fixation, processing, embedding in Epon, cutting ultrathin sections and contrasting with uranyl acetate and lead citrate for electron microscopy were performed according to standard techniques. The specimens were studied with a Jeol Jem 100 C electron microscope.

Results

Light microscopy. The most prominent growth pattern was non-cohesive sarcomatoid invasion (Fig. 2). Focally the cells were closely apposed to



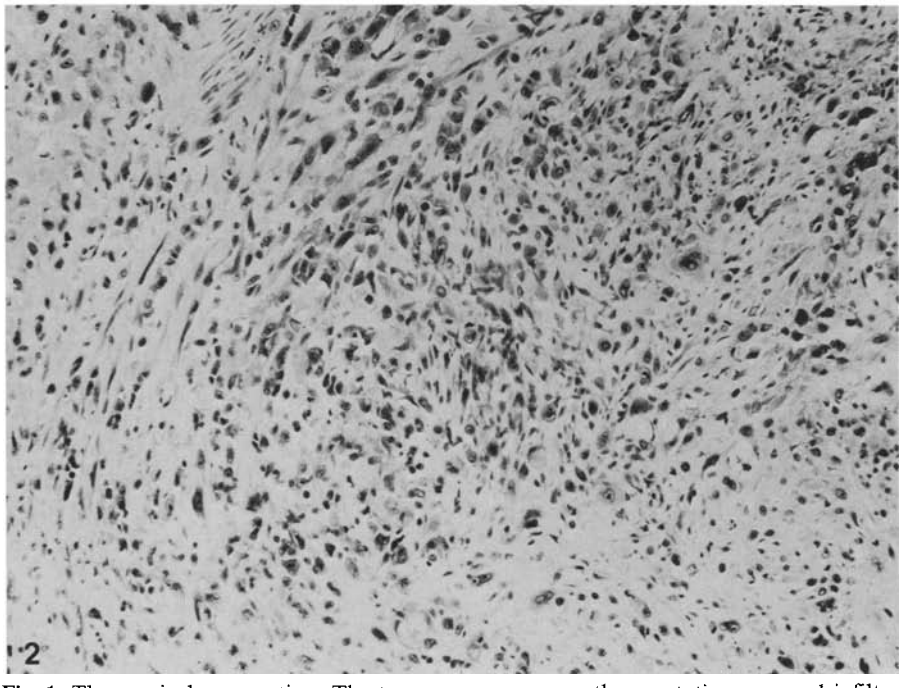


Fig. 1. The surgical preparation. The tumour encompasses the prostatic space and infiltrates both the vesical and rectal wall

Fig. 2. Sarcomatoid growth pattern. The stroma is focally loose and myxoid. v. Gieson, ×125

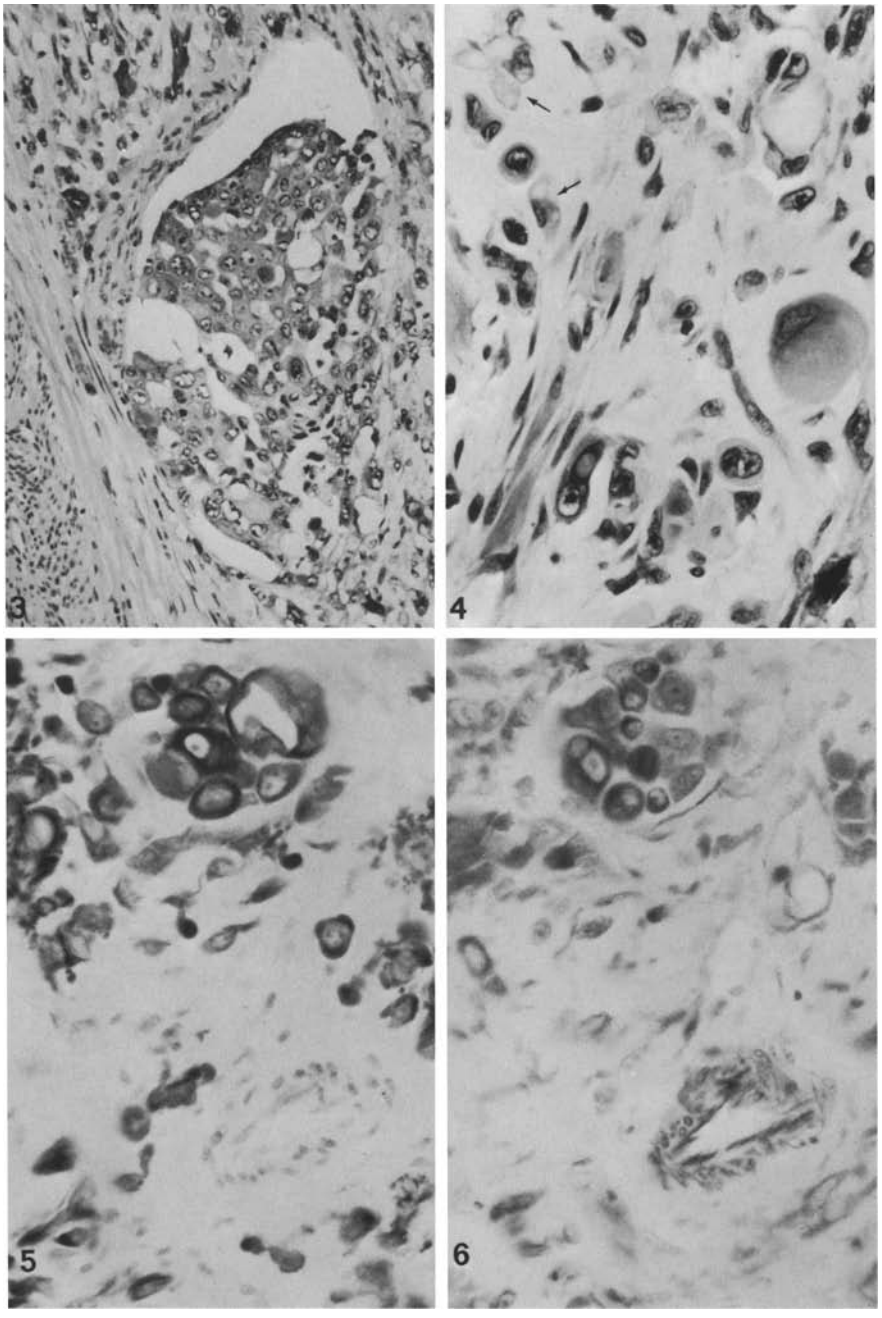


Fig. 3. A cohesive, intravascular cluster of tumour cells suggests epithelial neoplasia. v. Gieson, ×130

Fig. 4. Pleomorphic tumour cells. The large cell has homogenous cytoplasm, and a few cells contain intracytoplasmic empty vacuoles (*arrows*). v. Gieson, ×300

Fig. 5. Monoclonal anticytokeratin delineates the tumour cells invading smooth muscle. Immunoperoxidase, hematoxylin counterstain ×300

Fig. 6. The corresponding field as immunostained by monoclonal antivimentin. Arteriolar wall is also stained. Immunoperoxidase, hematoxylin counterstain ×300

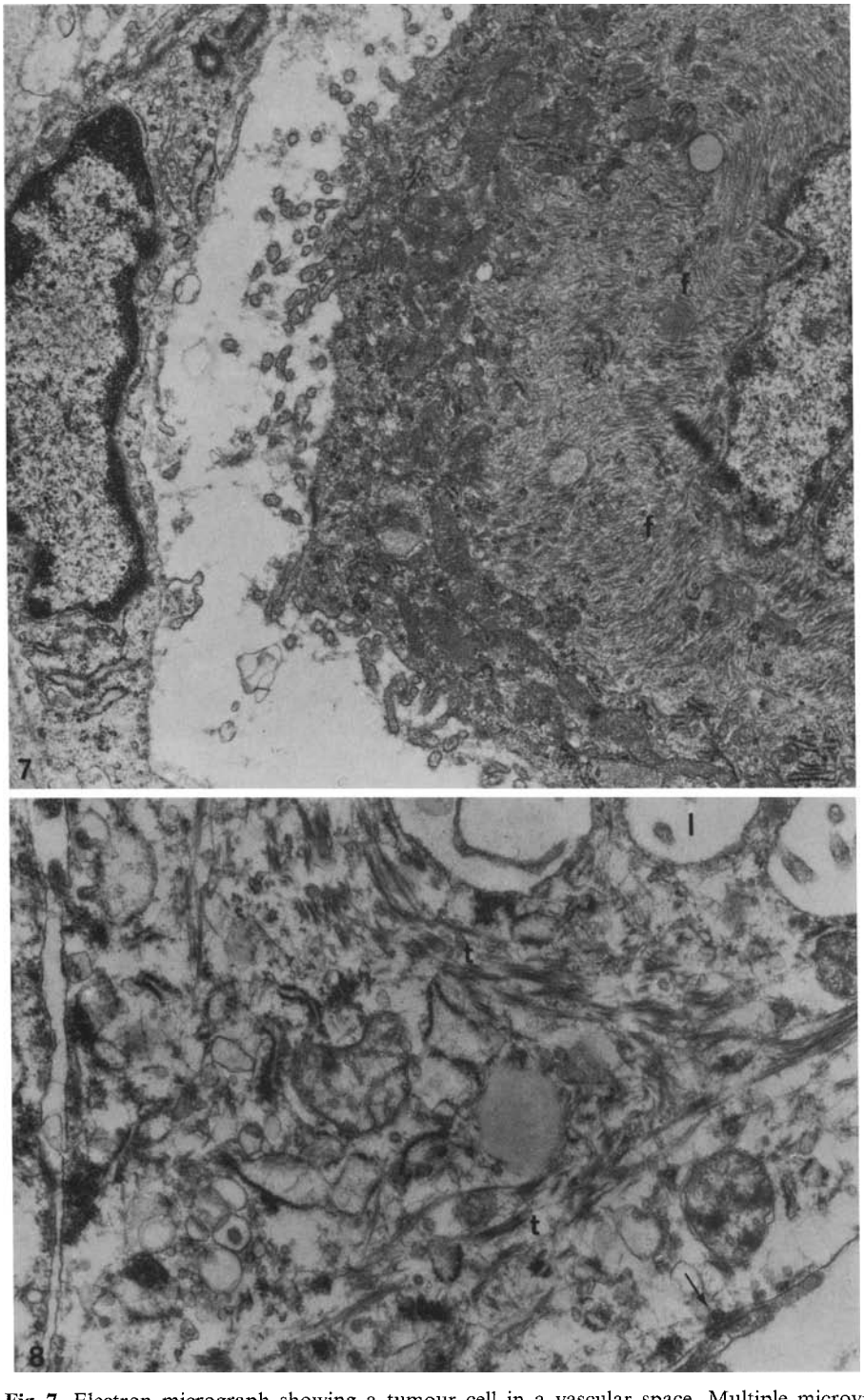


Fig. 7. Electron micrograph showing a tumour cell in a vascular space. Multiple microvilli are seen on the surface, and the cytoplasm contains a dense paranuclear meshwork of intermediate filaments (f). × 14,000

Fig. 8. Shieves of electron dense tonofilaments (*t*) in the peripheral cytoplasm. A few intracellular lumina (*l*) with sparse microvilli are demonstrated. Note also a cell junction (*arrow*). × 21,000

each other creating an epithelial appearance (Fig. 3). The cells were pleomorphic varying from fusiform to epithelioid with abundant eosinophilic cytoplasm. The vesicular nuclei contained large nucleoli. Mitoses and multinucleated cells were seen in moderate numbers. In the cytoplasm there was occasionally a homogenous paranuclear area, which was usually faintly PAS-positive, even after diastase pretreatment. Intracytoplasmic, empty-looking vacuoles were also seen (Fig. 4). No mucinous material, glycogen, cross striations or argyrophilia could be detected in the tumour cells, but the stroma was sometimes clearly myxoid containing material that stained intensively with Alcian blue.

Immunohistology. All tumour cells immunostained for cytokeratin (Fig. 5). The reaction for epidermal prekeratin was focally positive, but large groups of cells remained unstained. Anticarcinoembryonic antigen and antiepithelial membrane antigen also immunostained a proportion of tumour cells. Antivimentin gave a positive staining in practically all cells (Fig. 6). In contrast, the stainings for myoglobin, alfafetoprotein and lysozyme were negative.

Electron microscopy. The heterogenous morphology seen in light microscopy was substantiated by electron microscopic findings. The most conspicuous features were abundant microfilaments in the cytoplasm and microvilli on the cell surface. In occasional cells a paranuclear collection of intermediate-sized filaments corresponded to the inclusion-like material in light microscopy (Fig. 7). In the peripheral cytoplasm electron dense sheaves of tonofilaments were found. These were not related to the sparse macula adherens-type cell junctions. A few intracellular lumina with poorly developed microvilli were seen (Fig. 8). Granules interpreted as lysosomes and condensations of extracellular material along the cell membrane were scanty. No thick, myosin-like filaments, sarcomeres or secretory granules were detected.

Discussion

At the time of diagnosis, the tumour was located in the prostatic area. However, wide infiltration into the bladder and retrovesical tissues made the exact determination of the tissue of origin uncertain. The clinical presentation and the findings in routine light microscopy were compatible with a pleomorphic rhabdomyosarcoma. This diagnosis had to be rejected after the results of more specific methods became available.

Malignant rhabdoid tumour is a poorly differentiated and highly malignant neoplasm, which has been described recently as a separate entity (Haas et al. 1981). Almost all of them have been found in the kidney, but a few patients with extrarenal malignant rhabdoid tumour have been reported (Lemos and Hamoudi 1978; Gonzales-Crussi 1982). Those cases described by Hajdu (1979) as rhabdomyoblastoma may also include patients with malignant rhabdoid tumours.

Certain features of our patient and his neoplasm (the age of the patient,

location of the tumour, its pleomorphism and the presentation of microvilli) were not typical of a malignant rhabdoid tumour. However, the extended immunohistological analysis and the fine structure of the neoplasm disclosed following characteristics: (1) paranuclear collections of intermediate filaments, (2) absence of myoglobin and myofilaments, (3) coexpression of cytokeratin and vimentin and (4) positive staining for epithelial membrane antigen. On the basis of these findings we consider the neoplasm as an example of malignant rhabdoid tumour.

The theories concerning the histogenesis of malignant rhabdoid tumour vary considerably. While some authors favour the origin from neural crest (Haas et al. 1981) or histiocyte (Lemos and Hamoudi 1978; Gonzales-Crussi 1982), the others have suggested an epithelial derivation (Higa et al. 1984; Vogel et al. 1984). On the basis of the results of the present study we agree with the latter interpretation. We could not find any evidence of neurosecretory granules, phagocytosis or lysozyme, and lysosomes were few. Instead, the positive immunostaining for prekeratin, cytokeratin, epithelial membrane antigen and carcinoembryonic antigen as well as the microvilli, intracytoplasmic lumina, tonofilaments and cell junctions, though sparse, indicated all an epithelial differentiation. The demonstration of vimentin, the mesenchymal specific intermediate filament protein, in the tumour cells by us and by others (Rousseau-Merck et al. 1983; Vogel et al. 1984) seems to be at variance with this hypothesis. The coexpression of vimentin and cytokeratin has, however, been shown in carcinoma cells originating from the kidney (Holthöfer et al. 1983), thyroid gland (Miettinen et al. 1984), salivary gland (Caselitz et al. 1984), ovary (Miettinen et al. 1983) and in malignant effusions (Ramaekers et al. 1983). Therefore it appears likely that the expression of vimentin indicates either the primitiveness of malignant rhabdoid tumour or reflects dedifferentiating processes during carcinogenesis.

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