

Malignant rhabdoid tumour of the kidney: report of a case showing focal glomeruloid differentiation

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Abstract

A five-month-old male baby presented with an abdominal mass which was found on computerised tomography (CT) to be involving the left kidney. Nephrectomy and histopathological study showed morphological features of a malignant rhabdoid tumour. The tumour cells stained strongly for cytokeratin and epithelial membrane antigen and less intensely for vimentin. Electron microscopy revealed concentric whorled arrays of intermediate filaments within the tumour cell cytoplasm. The child was put on post-operative chemotherapy and radiotherapy but developed bilateral lung metastases and died three months after surgery.

Key words: Malignant rhabdoid tumour, kidney, cytokeratin, epithelial membrane antigen, desmin, myoglobin, glomeruloid differentiation.

INTRODUCTION

Malignant rhabdoid tumour (MRT), a rare and highly aggressive tumour affecting the infantile kidney¹ is characterized by a monotonous population of cells with eosinophilic cytoplasmic inclusions and macronucleoli.² Immunohistochemical stains consistently reveal positivity for a variety of cytokeratins, epithelial membrane antigen (EMA) and vimentin, and electron microscopy (EM) shows characteristic whorled filamentous structures that constitute the globular cytoplasmic inclusions.³ In recent years, immunocytochemical findings supporting a diverse phenotype, including epithelial, mesenchymal, myogenous and neuroectodermal phenotypes, have been reported⁴ and reports of extrarenal MRTs have created further controversy^{5,6} with regards its histogenesis. We wish to document a case of MRT in an infantile kidney which showed focal glomeruloid differentiation – yet another unusual phenotype.

CASE REPORT

A five-month-old Chinese male was referred to the University Hospital, Kuala Lumpur, for an abdominal mass that was accidentally discovered by the parents while bathing the infant. Physical examination revealed a 11 x 9 cm firm, fixed, hemispherical left lumbar mass. Computerised tomography (CT) of the abdomen revealed a 10 x 8 cm, heterogenous mass involving the lower pole of the left kidney with distortion of the pelvi-calyceal system. The liver showed no

abnormality. CT of the chest showed bilateral multiple small pulmonary nodules. At laparotomy, the mass was found to be adherent to the pancreas and the renal bed and the right and left para-aortic lymph nodes were enlarged. A left nephrectomy was performed and a pancreatic biopsy taken. Post-operatively, the child was administered combination chemotherapy consisting of vincristine, epirubicin, VP16, ifosphamide and mesna, and left renal bed irradiation (2400 Gy). Three months after surgery, a left supraclavicular lymph node became palpable and chest radiographs showed bilateral cannon ball secondaries. Abdominal CT showed no further local disease. The child rapidly deteriorated and died before any further chemotherapy could be instituted.

Pathology

The nephrectomy specimen measured 10 x 8 x 6 cm in size and showed a dark brown external surface. Cut sections revealed a greyish-white, fleshy, partly necrotic tumour mass replacing most of the kidney. A small rim of normal kidney tissue remained at the upper pole. Histology showed the tumour to be composed of monomorphous cells in diffuse pattern, sheets, cords and nests. Most of the cells showed a single prominent nucleolus and hyaline PAS-positive, intra-cytoplasmic globular inclusions (Fig 1). Six to eight mitoses could be seen in every high power field. In focal areas, tumour cells variously assumed a pseudoalveolar, interwoven fascicular or glomeruloid pattern

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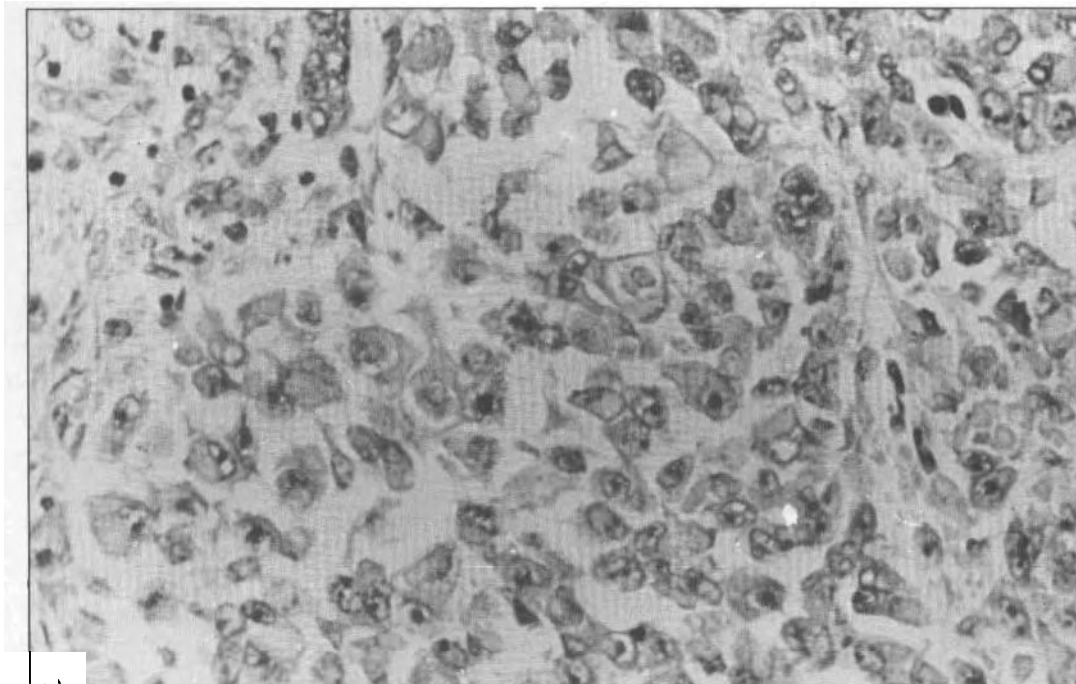


FIG. 1: Sheets of nucleolated tumour cells with hyaline cytoplasmic inclusions and macronucleoli. H&E X 400.

(Fig 2). The glomeruloid pattern was very distinctive with most of the tumour cells populating the glomeruloid structures showing PAS-positive cytoplasmic globules and single macronucleoli. These glomeruloid structures could be easily distinguished from residual non-neoplastic glomeruli that were trapped within the tumour. Numerous tumour cells were present in dilated lymphatic and vascular channels within the tumour. A few normal tubules and glomeruli were trapped among neoplastic cells. The renal capsule and adjacent pancreatic tissue were infiltrated by tumour.

Results of immunohistochemistry on paraffin-embedded tumour sections are summarized in Table 1. The tumour cells exhibited strong immunoreactivity for epithelial membrane antigen (EMA) and cytokeratin (MNF 116) (Fig.3). While EMA showed membrane positivity, MNF 116 decorated the cytoplasm of the cells, especially the inclusions. There was focal positivity for vimentin, desmin and myoglobin. The cells were not reactive for neuron specific enolase or S-100 protein.

Glutaraldehyde-fixed tumour tissue was postfixed in osmium tetroxide and epon-embedded for electron microscopy. Large oval tumour cells with eccentric, ovoid to indented nuclei and single macronucleoli were observed. The most distinctive feature was the presence of

cytoplasmic filamentous inclusions, composed of parallel filaments 6 to 9 nanometres in diameter, packed in concentric, whorled arrays and lying in juxtaposition to the nucleus (Fig 4).

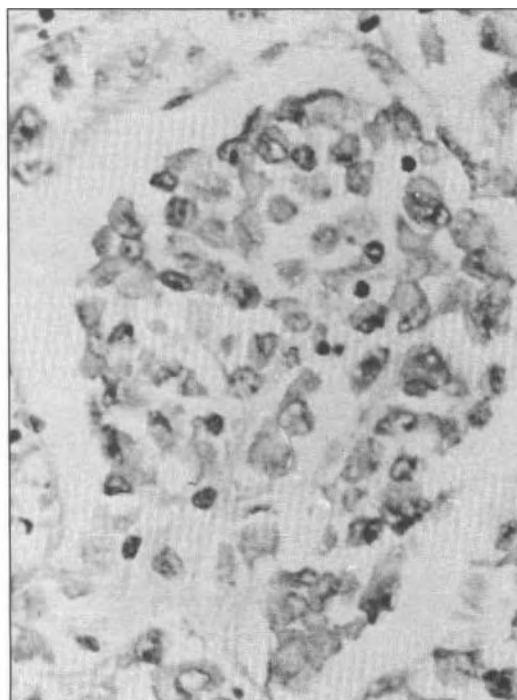


FIG. 2: MRTK cells aggregated into vague glomeruloid pattern. H&E X 300.

TABLE 1: Immunochemical expression by MRTK cells

Antibody	Specifications	Dilution	Technique	Results
EMA	DAKO (Monoclonal)	1: 600	ABC	Strongly +ve
MNF 116	DAKO (Monoclonal)	1: 400	ABC	Strongly +ve
Vimentin	DAKO (Monoclonal)	1: 300	ABC	Focal +ve
Desmin	DAKO (Monoclonal)	1: 80	ABC	Focal +ve
Myoglobin	DAKO (Polyclonal)	1: 2000	PAP	Focal +ve
NSE	DAKO (Monoclonal)	1: 800	ABC	Negative

ABC = Avidin biotin peroxidase complex method.
 PAP = Peroxidase antiperoxidase technique.

These were not membrane bound and occasionally incorporated cytoplasmic organelles such as lipid droplets or mitochondria. Membrane bound lipid vacuoles, glycogen, rough endoplasmic reticulum and lysosomes were also seen within the cytoplasm. Twisted or curved sheaves of filaments 10 nanometres or more in diameter resembling tonofilaments were present in a few of the cells but were not close to nexus type cell junctions that were occasionally present. Extracellular collagen was observed around tumour cells.

The pathological features were diagnostic of malignant rhabdoid tumour of the kidney (MRTK).

DISCUSSION

Concerned about the growing body of literature suggesting phenotypic diversity of MRT⁴ and the diagnosis of MRT being preferred for tumours arising at all ages, in many sites, and with diverse clinical outcomes, Weeks et al⁷ reviewed 111 cases of MRTK and 10 cases of extrarenal MRT from the National Wilms' Tumour Study Pathology Center. They concluded that, after excluding pseudorhabdoid tumours (which show some phenotypic features of MRTK), MRTK emerged as a separate entity with distinctive clinical, morphological and immunocytochemical features.

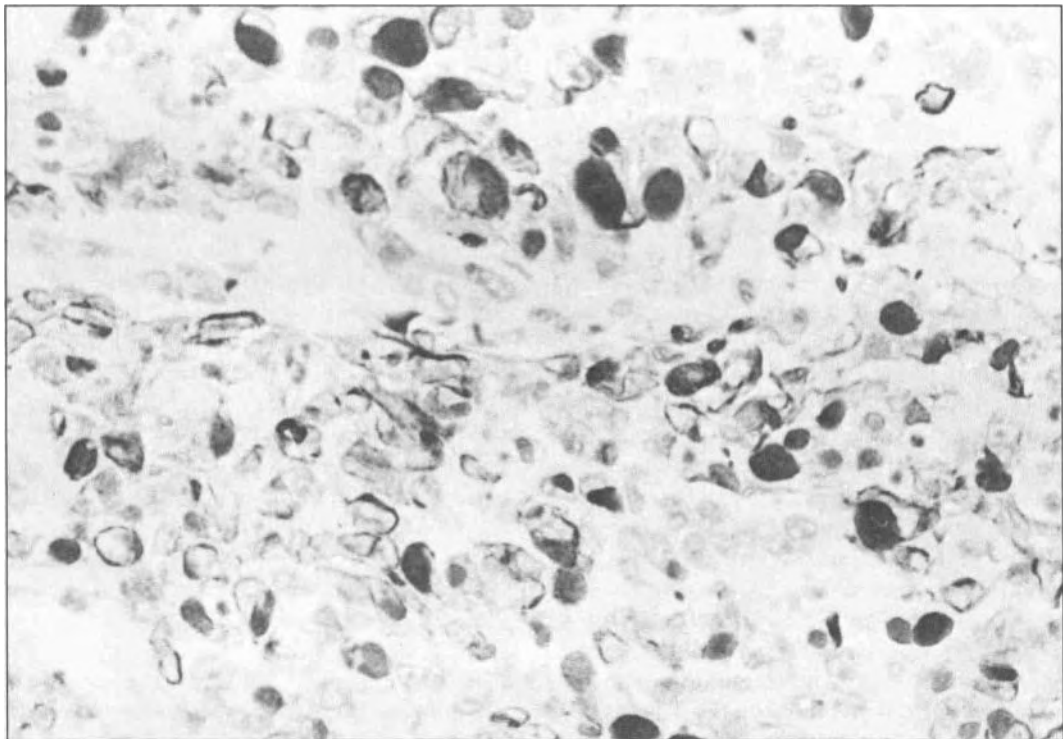


FIG. 3: Tumour cells showing cytoplasmic inclusions with strong immunoreactivity for MNF 116. Immunoperoxidase method for MNF 116 X400.

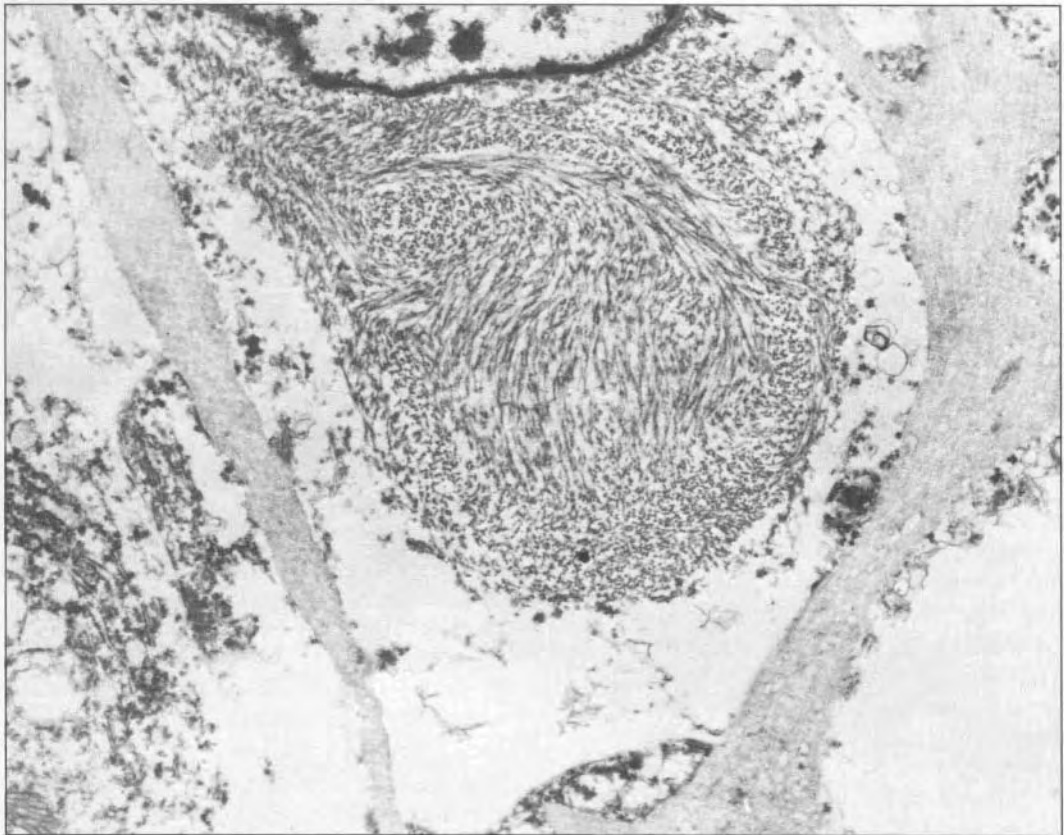


FIG. 4: Electron micrograph showing concentric whorled arrays of intermediate filaments in juxtannuclear position. X 10,400.

MRTK is among the most deadly tumours of infancy with a mortality rate exceeding 80%, even after aggressive multimodal therapy.¹ The present case shows the classical infantile onset and rapid lethal progression of the tumour as well as the characteristic light and electron microscopical features described in MRTK.^{2,3} Weeks *et al*⁸, describing pseudo-rhabdoid renal tumours, also warned against mistaking Wilms' tumour (WT) of favourable histology for MRTK, a mistake that could have disastrous therapeutic implications. The largely monotonous population of mitotically active cells with prominent nucleoli and cytoplasmic inclusions, and the total absence of a triphasic mixture of blastemal, embryonal and mesenchymal components and tubular differentiation are against the diagnosis of a WT. The aggressive clinical behaviour of this tumour is also unlike WT. Clear cell sarcoma of the kidney (CCSK), another rare childhood renal tumour, which shows a monotonous tumour cell population, also needs to be distinguished from MRTK.^{9,10} The former however, has clear rather than eosinophilic cytoplasm, and inconspicuous nucleoli.

The immunocytochemical reactions in this case were also compellingly in favour of MRTK. There was strong immunoreactivity for EMA and cytokeratin expressed in almost all the tumour cells, a phenomenon not expressed by CCSK cells or blastemal cells. Ultrastructurally, filamentous cytoplasmic inclusions were present in most of the cells but no rhabdomyoblastic differentiation was detected. These features dispell the possibility of CCSK and embryonal rhabdomyosarcoma.

The formation of focal glomeruloid structures in MRTK has so far not been documented. The cells forming glomeruloid structures were similar to the rest of the tumour in their intense positivity for EMA and cytokeratin, and their focal positivity for myoglobin. In our opinion, the presence of glomeruloid structures does not detract from a diagnosis of MRTK. However, such glomeruloid structures may indicate that MRTK cells still retain the capacity to differentiate along renal lines and in the context of histogenesis, MRTK may not be far different from Wilms' tumour. However, clinically it behaves as a more aggressive tumour with a

totally different biological behaviour, as also illustrated by this case.

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