Virchows Archiv A Pathol Anat (1989) 415:91–95

Virchows Archiv A
Pathological Anatomy and Histopathology

Case report

Carcinosarcoma of the urinary bladder

A light, immunohistochemical and electron microscopical case report

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Summary. A case of urinary bladder carcinosarcoma (UBCS) is reported with light, immunohistochemical and electron microscopical findings. The tumour consisted of a squamous cell carcinoma, variable spindle cell stromal elements compatible with fibrosarcoma, and rhabdomyoblasts. Intermediate filament co-expression of cytokeratin and vimentin was shown by immunohistochemistry. Electron microscopy (EM) confirmed the nature of the three components, and indicated some similarities between the three cell-types present. Comparisons with the previous UBCS in the literature are made.

Key words: Carcinosarcoma – Urinary bladder – Immunohistochemistry – Electron microscopy – Rhabdomyoblast

Introduction

The vast majority of malignant bladder tumours are of epithelial derivation (carcinoma) whilst only a tiny minority are of mesenchymal origin (sarcoma). Even rarer are bladder tumours with both malignant epithelial and mesenchymal elements. Only 38 cases of such carcinosarcomas have been documented in the English literature (Young 1987), mostly detailed in terms of clinical aspects and conventional light microscopy. Fromowitz et al. (1984) and Grossman et al. (1984) have immunophenotyped UBCS while Duong et al. (1981), Murao and Tanahashi (1985) and Grossman et al. (1984) have used electron microscopy. We present here a primary carcinosarcoma of the urinary bladder characterised by light, immunohistochemical and electron microscopy.

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Case history

A 69 year old white female presented with a recent history of cystitis and supra-pubic pain. She smoked 20 cigarettes a day, and had never received radiotherapy. Clinical examination was unremarkable. An intravenous pyelogram revealed a large mass within the bladder, with normal ureters and kidneys bilaterally. Cystoscopy confirmed the tumour, arising from the trigone and bladder base. Histology of the transurethrally resected tumour tissue showed it to be a carcinosarcoma. Post-operative radiology showed residual intra-vesical tumour with no extension beyond the bladder. An anterior pelvic clearance and ureteroileostomy was performed. 24 months post-operatively the patient remains well with no recurrent disease and normal renal function.

Materials and methods

Tissues from both the transurethral and pelvic clearance operations were routinely processed into paraffin wax, sectioned at 5 μm and stained with Haematoxylin and Eosin (H & E). Selected slides were stained by the avidin-biotin technique with Cam 5.2 (Becton-Dickinson), for vimentin, desmin, myoglobin, S100 protein and high molecular weight cytokeratin (HMW-CK) (all Dako), the last five with and without prior trypsinisation. Material for electron microscopy was conventionally processed into epoxy resin.

Results

Light microscopy

The cystoscopic "chippings" of the tumour consisted of two distinct but intimately admixed components (Fig. 1A). A large-cell, focally keratinising, moderately well differentiated squamous cell carcinoma, with an apparent origin from an in situ surface component was set within, but distinct from, a stroma of varying appearance (Figs. 1A–C). In some areas the stroma was loose and myxoid, with widely spaced stellate cells and spindle cells, with scanty cytoplasm and spindle or polygonal nuclei. Elsewhere the stroma was composed

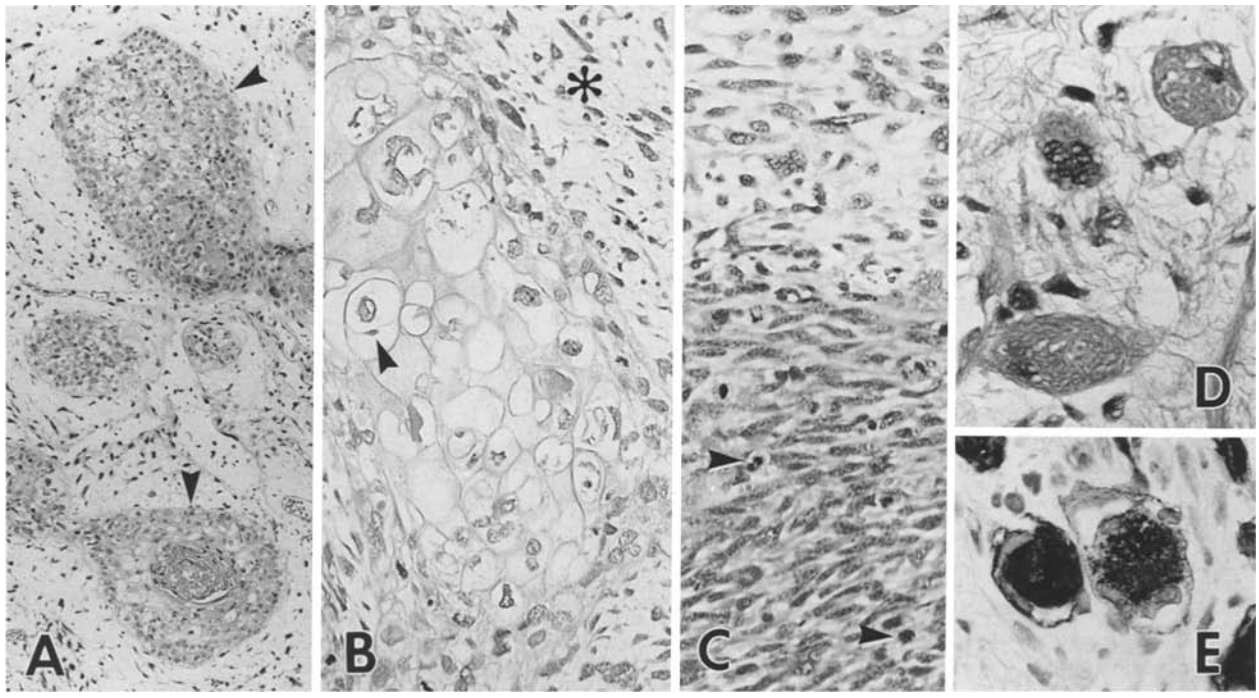


Fig. 1. (**A**) Light micrograph showing islands of squamous carcinoma (*arrowheads*) set in a loosely textured spindle cell sarcomatous component (H & E, ×25). (**B**) Island of carcinoma (consisting of cells with rounded to oval nuclei) surrounded by sarcomatous component (*). Note abundant clear cytoplasm of carcinoma cells (*arrowhead*) (H & E, ×65). (**C**) Spindle cell sarcomatous component showing areas of differing cellularity. Note numerous mitoses (*arrowheads*) (H & E, ×65). (**D, E**) Rhabdomyoblasts in H & E section (**D**, ×250) and after staining for desmin (**E**, ×250)

of well defined areas of tightly packed spindled cells with a focal storiform pattern, having scanty cytoplasm, oval nuclei and frequent mitoses (Fig. 1C), reminiscent of a fibrosarcoma. Within the looser stromal areas were plump, round or strap-like cells, with eosinophilic cytoplasm which had cross-striations, consistent with rhabdomyoblasts (Fig. 1D). No other carcinomatous or sarcomatous elements were identified.

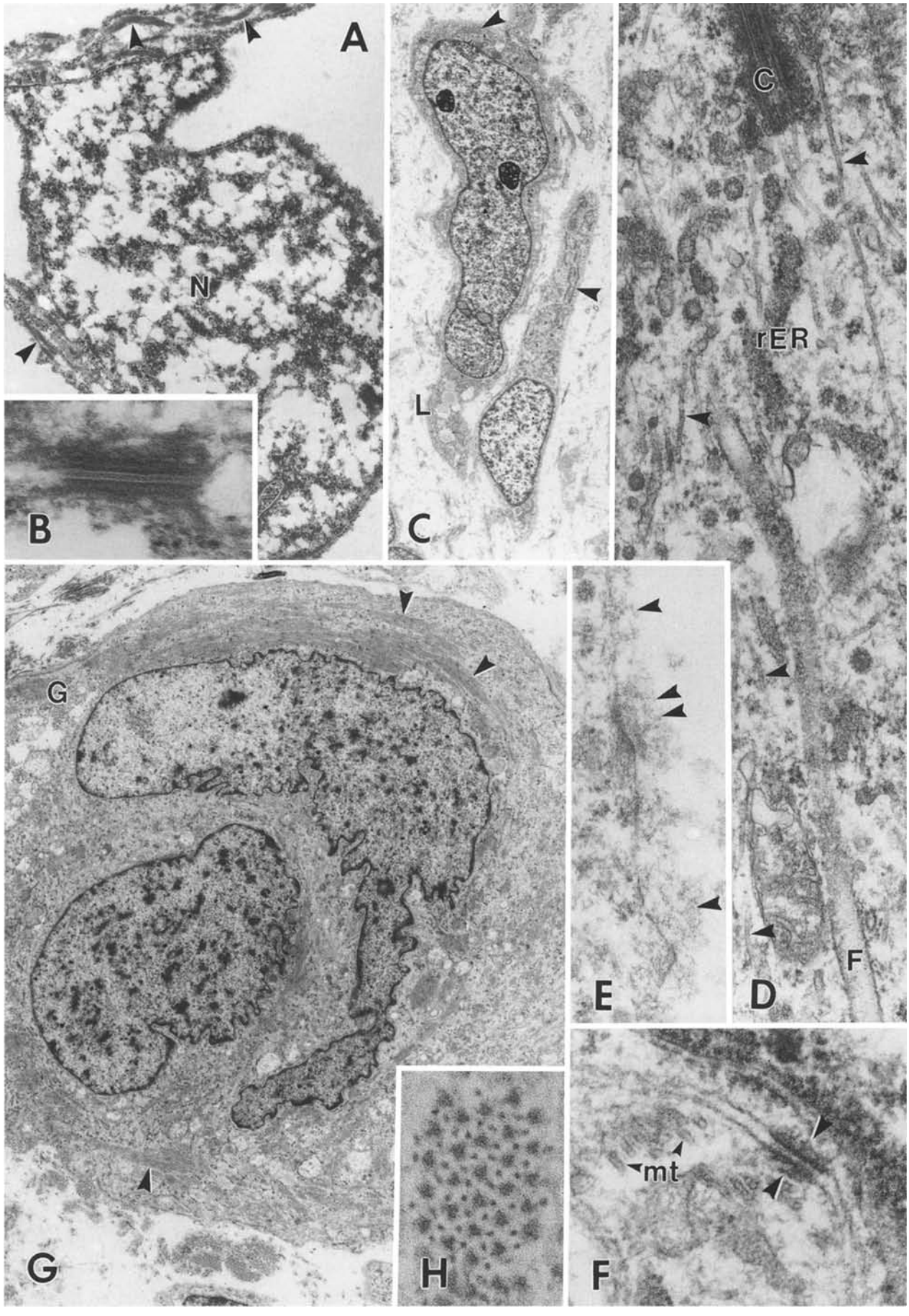
The operative pelvic clearance specimen consisted of the bladder, uterus (with attached adnexae) and several pelvic lymph nodes. The bladder contained a polypoidal bosselated tumour, 10.0 × 7.5 × 5.0 cm, arising from a narrow base just above, and posterior to, the internal urethral meatus. On section it was yellow/white with varying myxoid and haemorrhagic foci. The bladder wall appeared uninvolved by tumour. The other tissues were of normal appearance both grossly and histologically.

By light microscopy, the tumour exhibited the same features as the initial biopsy, with the bladder wall origin confirmed. The bladder mucosa away from the polyp showed a cystitis cystica and follicularis pattern, with squamous metaplasia merging into that of the neoplastic epithelium overlying the polyp. Multiple blocks failed to show any other tumour component or extra-vesical spread.

Immunohistochemistry

Immunohistochemistry on cystoscopic and pelvic-clearance specimens gave identical results. The

Fig. 2. Electron microscopy of carcinomatous (**A, B**) and sarcomatous (**C–H**) components. (**A**) Nucleus (N) containing many small blocks of heterchromatin and with minor invaginations of envelope. A narrow perinuclear rim of organelles includes tonofibrils (*arrowheads*) (×12000). (**B**) macula adhaerens (×83000). (**C**) fibroblastoid cells with narrow perinuclear rim of cytoplasm extending as broad polar processes. Note heterochromatin dispersed in small pieces. Lipid, L; rER (*arrowheads*) (×28000). (**D**) Spindle cell cytoplasm containing microtubules (*arrowheads*), centriole (**C**), rER and a collagen fibril (**F**) (×48000). (**E**) Surface features of fibroblastoid spindle cell – a fuzzy coat (*arrowheads*) and subplasmalemmal density with denser surface coating (*double arrowheads*) are apparent (×53000). (**F**) Simple junction (*arrowheads*) and microtubules (mt) in a cell process (×83000). (**H**) Rhabdomyoblast (**G**, ×5100) showing fine nuclear indentations and heterochromatin speckling. Abundant cytoplasm contains glycogen pools (**G**) and myofilament bundles (*arrowheads*). Thick and thin filaments in cross section (**H**, 112000)


A
N
B
C
L
C
rER
D
F
E
G
G
H
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squamous carcinoma (both in situ and infiltrative) was positive for both the cytokeratins, with occasional cells in the infiltrative components being vimentin positive. The stromal cells (both 'loose' and tightly packed spindle cells) were vimentin positive, with occasional cells (mostly in the spindled areas) being either Cam 5.2 or HMW-CK positive. The rhabdomyoblasts were desmin (Fig. 1E), myoglobin and vimentin positive. S100 protein was negative throughout.

Electron microscopy

Nuclei in the epithelial component contained many small blocks of heterochromatin (Fig. 2A). Cytoplasm contained numerous monoribosomes, moderate numbers of rough endoplasmic reticulum cisternae (rER) and plentiful dense tonofibrils (Fig. 2A), some abutting on macula-adhaerens-type junctions (desmosomes) (Fig. 2B).

The sarcomatous cells of the 'loose' areas were set in a light matrix containing proteoglycan-like granules and little collagen (Fig. 2C). Nuclei had minor indentations, small numbers of moderately sized nucleoli, and diffusely distributed pieces of heterochromatin. The cytoplasm formed a thin envelope around the nucleus, and had broad polar processes (Fig. 2C). Mono- and poly-ribosomes and Golgi were prominent. An occasional cytoplasmic collagen fibril was seen (Fig. 2D). Close cell-to-cell apposition was noted with an occasional simple junction and subplasmalemmal densities (Figs. 2E, F). A distinct external lamina was absent but a fuzzy coat invested the cells (Fig. 2E).

Rhabdomyoblasts contained variable numbers of thick (18–22 nm) and thin (6–7 nm) filaments but no Z disks (Figs. 2G, H). A fuzzy external coat surrounded solitary cells or covered the external surfaces of cell clusters; it was absent from closely apposed surfaces within clusters where primitive junctions were found. Conspicuous lipid amid lakes of glycogen was noted. Nuclei had a similar heterochromatin speckling and nucleolar complement of the spindled cells.

Despite numerous blocks, no areas of carcinoma/sarcoma interface or of tightly packed spindle cells were found.

Discussion

Previously reported urinary bladder carcinosarcomas (UBCS) have been few in number and have varied considerably in the degree of documentation of their histopathological appearances. Three studies report electron microscopy findings (Duong et al. 1981; Murao and Tanahashi 1985; Grossman et al. 1984) and only two immunohistochemistry (Fromowitz et al. 1984; Grossman et al. 1984). The case presented here, in using both immunohistochemistry and EM, is a detailed example of a UBCS, containing a squamous carcinomatous element in combination with a sarcomatous component characterised by fibrosarcomatous and rhabdomyoblastic features.

The light microscopy findings fulfil the criteria of a carcinosarcoma, with malignant epithelial and mesenchymal elements intimately admixed but separate from each other (Young 1987). The light findings agree with previous reports of UBCS, which found squamous carcinoma in 18% and skeletal muscle differentiation in 24% of cases. This refutes the AFIP statement that rhabdomyoblasts have not been found in UBCS (AFIP 1975).

Immunohistochemistry in UBCS is limited to two reports. Grossman et al. (1984) reported a transitional cell carcinoma, with a poorly documented spindle cell sarcomatous component, in which some cells had cross-striations and were myoglobin positive. Fromowitz et al. (1984) described an in situ and infiltrating transitional cell carcinoma with areas of adenocarcinoma, and others of high grade chondrosarcoma; all three elements were set within a non-differentiated malignant spindle cell component with a storiform pattern. This case had keratin positivity within the epithelial and spindle cell areas but inconclusive S100 protein positivity. Our results confirm both of these positive findings within the same tumour, and demonstrate intermediate filament co-expression within tumour cells in both components. This duality of immunostaining is similar to that reported in many other tumours including uterine mixed mesodermal tumours (UMMT) (Geisinger et al. 1987).

Ultrastructural accounts of UBCS are confined to three reports. The squamous differentiation in our case contrasts with the transitional cell carcinoma recorded by Duong et al. (1981) and Grossman et al. (1984), and the adenocarcinoma of Murao and Tanahashi (1985). The sarcomatous element also differs. The case of Murao and Tanahashi (1985) lacked rhabdomyoblasts; conversely, their osteochondrosarcomatous component was absent from our material. However, 10% of their sarcomatous component consisted of undifferentiated tissue which was similar in having a 'fibroblastoid' phenotype (plentiful rER, well developed Golgi and simple junctions). The presence of intracellular collagen in our case reinforces the interpretation of a fibroblastoid phenotype for the spindle

cell component which may therefore be designated as fibrosarcomatous. Duong et al. (1981) also found bone and cartilage formation in the sarcomatous portion of the tumour. This was set in a malignant mesenchymal tissue consisting of cells with chondrocytic features and others with large irregular nuclei and abundant rER. However, the ultrastructural description is too brief to allow a detailed comparison, as is that in the report of Grossman et al. (1984). The latter describe a mix of pleomorphic and spindle cells, some of which contained cross-striations by light microscopy, and sarcomeres and Z disks by electron microscopy. However, it is unclear to which cell-type (spindle or pleomorphic) they are referring. Our rhabdomyoblasts were unambiguously rounded cells and not spindled.

Some points of detail deserve mention. The subplasmalemmal densities and simple junctions described here are typical fibroblastic or mesenchymal features (Eyden et al. 1986; Dickersin 1987). The prominent microtubules (also described, for example, in a solitary Schwannoma – Erlandson and Woodruff 1982) should not, in this case, be construed as another line of sarcomatous differentiation, more so given the negative staining for S100 protein. Some microtubules contact centrioles and may therefore be spindle remnants in this mitotically active neoplasm. The rhabdomyoblasts in this case are as previously reported in UMMT (Bocker and Stegner 1975). The spindle cell component is also similar to that in UMMT, to judge from the data of Geisinger et al. (1987), although here convincing evidence for fibroblastic differentiation was lacking.

As this case and the others in the literature show, UBCS are histologically diverse. The evidence to date does not allow a definitive statement as to histogenesis. The immunohistochemistry can be argued to favour either a dual cell, or a metaplastic single cell, origin, with the nuclear similarity by EM of the carcinomatous and sarcomatous components possibly favouring the latter. However, we would be cautious about extrapolating histogenesis from phenotypic data. Detailed studies on these rare tumours such as presented here may, however, shed further light on the lines of subcellular differentiation and hence the nature of UBCS.

Acknowledgements. We would like to thank Alan Curry for assistance with some of the light micrographs, Daxa Chauhan and Julie Cook for technical help in electron microscopy, and Joan Unwin for secretarial assistance.

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Received December 20, 1988 / Accepted March 3, 1989