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Comparative immunohistochemistry of malignant fibrous histiocytoma and sarcomatoid carcinoma of the urinary tract

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Summary. An immunohistochemical analysis using antibodies to cytokeratin, epithelial membrane antigen, alpha-1-antitrypsin, alpha-1-antichymotrypsin and factor XIIIa was performed in four cases of malignant fibrous histiocytoma and five cases of sarcomatoid carcinoma in the urinary tract. All cases of malignant fibrous histiocytoma showed positive staining for factor XIIIa, alpha-1-antitrypsin and alpha-1-antichymotrypsin. No case was positive for factor XIIIa, but one case with sarcomatoid carcinoma stained positive for alpha-1-antitrypsin and alpha-1-antichymotrypsin. All cases showed positive staining for cytokeratin and 4 cases with sarcomatoid carcinoma were positive for epithelial membrane antigen, but no cases with malignant fibrous histiocytoma were positive. Immunohistochemical analysis would thus help to distinguish malignant fibrous histiocytoma from sarcomatoid carcinoma of the urinary tract.

Key words: Malignant fibrous histiocytoma – Sarcomatoid carcinoma – Urinary tract – Immunohistochemistry

Malignant fibrous histiocytoma (MFH) of the urinary tract is a rare tumor. Sarcomatoid carcinoma of the urinary tract showing proliferation of cancer cells in storiform pattern or interlacing sheets is a variant of invasive transitional or squamous cell carcinoma [9]. The distinction between MFH and sarcomatoid carcinoma is important for both urologists and pathologists. The difficulties in differentiating betwen MFH and sarcomatoid carcinoma in a conventional microscopic study prompted us to clarify the pathological features by immunohistochemical analysis, using antibodies to cytokeratin, epithelial membrane antigen, alpha-1-antitrypsin, alpha-1-antichymotrypsin, and factor XIIIa. We refer to the distinction of immunopathological features between MFH and sarcomatoid carcinoma in the urinary tract.

Materials and methods

The surgical pathology files of the Miyazaki Medical College were surveyed to retrieve all available examples of MFH and sarcomatoid carcinoma in the urinary tract. Tissue samples fixed with 10% formalin were routinely embedded in paraffin. The blocks were cut into 3-μm-thick serial sections. After deparaffinization with xylol and alcohol, these sections were stained with hematoxylin and eosin (H&E). Adjacent paraffin sections were mounted on glass slides coated with poly-L-lysine to be used for immunohistochemical analysis. The sections were pretreated with absolute methanol, freshly prepared 0.3% with H_2O_2, for 30 min in order to block the endogenous peroxidase activity of the cells. Primary antibodies against cytokeratin, epithelial membrane antigen, alpha-1-antitrypsin, alpha-1-antichymotrypsin (Dako, Glostrup, Denmark) and factor XIIIa (Behringwerke, Marburg, Germany) were applied at a dilution of 1:50 to 1:200. The avidin-biotin-peroxidase complex method [7] with Vectastain ABC kits (Vector laboratories, Burlingame, Calif.) was used thereafter. The development of the peroxidase reaction was performed by incubating sections in 3,3′-diaminobentidine solution with 0.005% H_2O_2 for a maximum of 10 min. They were counterstained with Harris hematoxylin. Reactions for immunostains were graded as positive only if dark, granular precipitates of chromogen were observed diffusely in the tumor cells. These results were then compared with the findings in H&E preparations.

Results

The clinical features of four cases of MFH and five cases of sarcomatoid carcinoma are summarized in Table 1. Microscopic features of all cases with MFH were of a storiformpleomorphic subtype described by Enzinger and Weiss [3] (Fig. 1). Those of sarcomatoid carcinoma showed proliferation of spindle or pleomorphic tumor cells in a storiform pattern and small foci of cancer cells sparsely distributed (Fig. 2). It is difficult to differentiate sarcomatoid carcinoma from MFH in H&E preparations alone.

The results of comparative immunohistochemical study of four cases of MFH and five cases of sarcomatoid carcinoma are listed in Table 2. All four cases of MFH stained positive for tumor cells at immunohistochemical

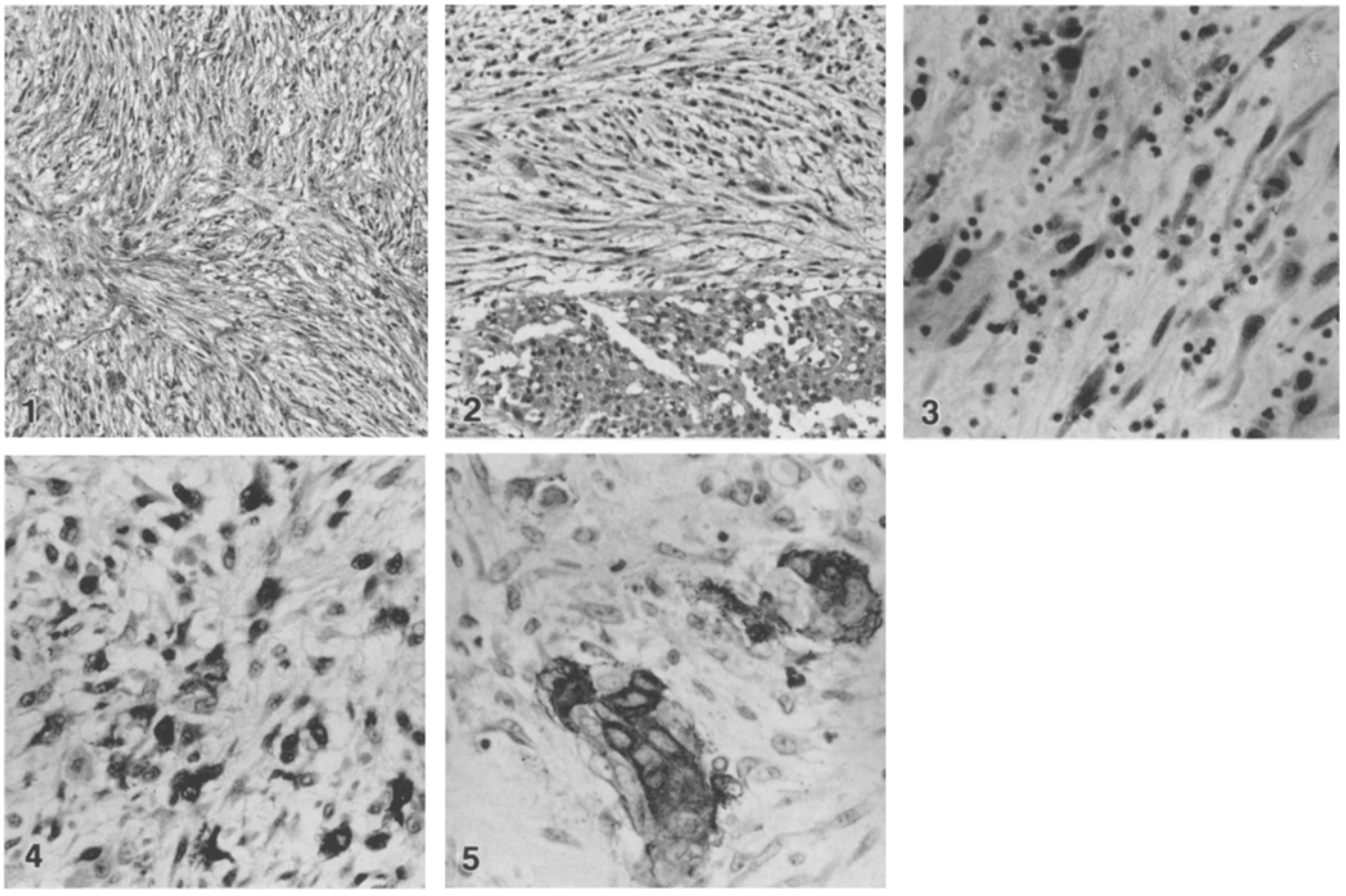

Fig. 1. Malignant fibrous histiocytoma. Pleomorphic fibroblastlike spindle cells proliferate in storiform pattern (H&E, ×100)

Fig. 2. Sarcomatoid carcinoma. A focus of polygonal cancer cells is evident in the lesion composed of spindle cells (H&E, ×150)

Fig. 3. Malignant fibrous histiocytoma. Positive staining for alpha-1-antichymotrypsin is seen (immunoperoxidase stain, ×340)

Fig. 4. Malignant fibrous histiocytoma. Positive staining for factor XIIIa is noted (immunoperoxidase stain, ×340)

Fig. 5. Sarcomatoid carcinoma. Positive staining for cytokeratin is found (immunoperoxidase stain, ×340)

analysis for alpha-1-antitrypsin, alpha-1-antichymotrypsin (Fig. 3) and factor XIIIa (Fig. 4). All spindle and giant cells in tumor were positive for these antigens. None of them stained positive for cytokeratin and epithelial membrane antigen.

All five cases of sarcomatoid carcinoma stained positive for cytokeratin (Fig. 5), as did four for epithelial membrane antigen. All epithelial tumor cells in small foci and sparse spindle cells were positive for these antigens. In one case, sarcomatoid carcinoma stained positive for alpha-1-antichymotrypsin. None of them expressed factor XIIIa.

Discussion

Sarcomatoid carcinoma has been also referred to as pseudosarcoma, carcinoma with pseudosarcomatous stroma, metaplastic carcinoma, and spindle cell carcinoma [9, 16]. In most instances, they are recognized as carcinomas because of a microscopic association with conventional invasive or in situ components [14]; however, tumors that lack such elements or have only minor foci may be difficult to distinguish from MFH. Actually, sections stained with H&E show that tumor cells of sarcomatoid carcinoma are arranged in a storiform pattern, as are those of MFH. It is essential to examine many sections and search for small foci of cancer cells in sarcomatoid carcinomas in order to differentiate between them.

Immunohistochemically, sarcomatoid tumor manifesting cytokeratin or epithelial membrane antigen is considered to be epithelial in nature. Weiss et al. [16] reported a case of MFH expressing cytokeratin, thus suggesting that cytokeratin itself should not be a marker to distinguish sarcomatoid carcinoma from MFH. Wick et al. [17] reported that cytokeratin and epithelial membrane antigen were positive in all cases of sarcomatoid carcinoma. In our study, however, one case of those tumors did not stain for epithelial membrane antigen. This result may indicate that not all sarcomatoid carcinomas express an epithelial membrane antigen.

Table 1. Clinical features of four cases of malignant fibrous histiocytoma and five cases of sarcomatoid carcinoma of the urinary tract

Case	Age/Sex	Final diagnosis	Location of lesion	Symptoms/signs	Therapy	Outcome
1	55/M	MFH	Bladder	Hematuria	XRT; CTX	DOD: 9 months
2	66/F	MFH	Bladder	Hematuria	None	DOO: 2 months
3	76/M	MFH	Renal pelvis	Flank mass	Nephroureterectomy	DOD: 12 months
4	61/M	MFH	Renal pelvis	Hemorrhage from nephrostomy	Nephrectomy	DOD: 5 months
5	76/M	Sarcomatoid CA	Bladder	Hematuria	Cystectomy	AWD: 4 months
6	68/F	Sarcomatoid CA	Bladder	Hematuria	Cystectomy; CTX	DOD: 3 months
7	76/M	Sarcomatoid CA	Bladder	Hematuria	TUR	NED: 7 months
8	61/M	Sarcomatoid CA	Ureter	Frank pain/ ureteral stone	Nephroureterectomy	NED: 9 months
9	74/F	Sarcomatoid CA	Renal pelvis	Hematuria	Nephroureterectomy	DOD: 18 months

MFH, Malignant fibrous histiocytoma; CA, carcinoma; TUR, transurethral resection; XRT, radiotherapy; CTX, chemotherapy; DOD, died of disease; DOO, died of other disease; AWD, alive with disease; NED, no evidence of disease

Table 2. Results of immunoperoxidase staining in malignant fibrous histiocytoma and sarcomatoid carcinoma of the urinary tract

Tumor	*n*	CK	EMA	AT/ACT	F-XIIIa
MFH	4	0	0	4	4
Sarcomatoid CA	5	5	4	1	0

MFH, Malignant fibrous histiocytoma; CA, carcinoma; CK, cytokeratin; EMA, epithelial membrane antigen; AT, alpha-antitrypsin; ACT, alpha-1-antichymotrypsin; F-XIIIa, factor XIIIa

In our series, all cases of MFH stained positive for factor XIIIa, alpha-1-antitrypsin, and alpha-1-antichymotrypsin. MFH is thought to possibly originate from primitive mesenchymal cells that show partial histiocytic and fibroblastic differentiation [3]. Alpha-1-antitrypsin and alpha-1-antichymotrypsin have been observed in epithelial cells [2, 8], suggesting that alpha-1-antitrypsin and alpha-1-antichymotrypsin are not specific markers for MFH. Nemes et al. [13] have recently reported that factor XIIIa-positive cells in MFH were fibrohistiocytic precursors. Our data show that factor XIIIa is one of the useful immunohistochemical markers for MFH.

Only seven cases of MFH of the urinary tract have been reported [1, 4–6, 11, 12, 14]. Koss [10] stated that cases reported by Anderson et al. [1] and Henriksen et al. [6] should be regarded as sarcomatoid carcinoma. A histological distinction between MFH and sarcomatoid carcinoma is difficult, because spindle cells of both tumors are arranged in a storiform pattern. In our study, sparse spindle cells of sarcomatoid carcinoma stained positive in five cases for cytokeratin and in four of five cases for epithelial membrane antigen, while spindle cells of MFH were negative. Spindle cells of sarcomatoid carcinoma stained negative for factor XIIIa and were positive for alpha-1-antitrypsin and alpha-1-antichymotrypsin in one case. All spindle and giant cells of MFH were positive for factor XIIIa, alpha-1-antitrypsin, and alpha-1-antichymotrypsin. Using these results, we were able to distinguish MFH from sarcomatoid carcinoma. The immunohistochemical analysis for these antigens, together with careful conventional morphological examination, is very useful for the differentiation between MFH and sarcomatoid carcinoma in the urinary tract.

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