

Pseudosarcomatous Myofibroblastic Tumor and Myosarcoma of the Urogenital Tract

Immunohistochemical Characteristics and Differential Diagnosis

Kazuo Watanabe, MD; Keiich Baba, MD; Atsuko Saito, MD; Nobuo Hoshi, MD; Toshimitsu Suzuki, MD

● **Objective.**—Pseudosarcomatous myofibroblastic tumors (PMTs) of the urogenital tract are rare but distinctive lesions. Despite their benign behavior, they are frequently misinterpreted as leiomyosarcomas and rhabdomyosarcomas in preoperative biopsies and even in resected specimens because of their atypical spindle-cell features. Precise diagnosis of PMTs is important to avoid unnecessary radical therapy. We analyzed urogenital myoid tumors to clarify which of their characteristics are useful for the differential diagnosis.

Methods.—We evaluated 7 urogenital myoid tumors consisting of 3 PMTs, 2 leiomyosarcomas, and 2 rhabdo-

Pseudosarcomatous myofibroblastic tumor (PMT) is a distinctive lesion in the urogenital tract. Since the first report by Roth,¹ various designations have been applied to this lesion including postoperative spindle cell nodule,² inflammatory pseudotumor,^{3,4} pseudosarcomatous fibromyxoid tumor,⁵⁻⁷ nodular fasciitis,⁸ pseudosarcomatous myofibroblastic proliferation,⁹ and pseudosarcomatous myofibroblastic tumor.¹⁰ However, it is still unclear whether this lesion is a neoplastic or reactive condition.¹¹⁻¹⁶ The prognosis of PMT is excellent,^{4,6,9,10} and spontaneous regression has even been reported.¹⁷ Despite this favorable clinical behavior, PMT is commonly composed of atypical spindle cells that may be easily misinterpreted as cells of leiomyosarcoma or rhabdomyosarcoma.^{9,10} We analyzed 7 cases of urogenital myoid tumors including 3 PMTs, 2 leiomyosarcomas, and 2 rhabdomyosarcomas using a variety of immunohistochemical muscle markers.

MATERIAL AND METHODS

The cases for this study were obtained from the files of the Pathology Division, Fukushima Medical University School of Medicine Hospital and the Jusendo General Hospital and had been histologically diagnosed as myogenic mesenchymal tumors (Table). Two of the PMT cases (cases 1 and 2) were described brief-

ly in a previous report.¹⁸ Tissue sections were prepared from paraffin blocks and stained with hematoxylin-eosin. The streptavidin-biotin-peroxidase complex method (SABC kit, Dako, Kyoto, Japan) was used for immunohistochemistry. Staining was performed with primary antibodies to desmin (D33, Dako; 1:50), α -smooth muscle actin (α -SMA) (Dako; 1:200), muscle-specific actin (MSA) (HHF35, Enzo Diagnostics, New York, NY; 1:8000), high-molecular-weight (h-)caldesmon (h-CD, Dako, Kyoto, Japan, 1:50), and myogenin (Myf4) (LO26, Novocastra, Newcastle, UK; 1:50). Microwave pretreatment was performed for desmin, h-caldesmon, and myogenin immunostaining. The immunoreactive products were visualized by diaminobenzidine. Nuclei were counterstained with hematoxylin.

Results.—Desmin, muscle-specific actin, and α -smooth muscle actin were noted variably in all tumor types, whereas high-molecular-weight caldesmon was expressed only in leiomyosarcomas, and myogenin was expressed only in rhabdomyosarcomas.

Conclusion.—High-molecular-weight caldesmon and myogenin are useful for differentiating urogenital PMTs from myosarcomas.

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RESULTS

Clinical Features

The clinical data for the 7 cases are listed in the Table. All of the patients with PMT had bladder lesions and had undergone partial cystectomy with or without adjuvant chemotherapy, and all were alive from 6 to 13 years later without recurrence. The original diagnoses were leiomyosarcoma, leiomyoma, and rhabdomyosarcoma. No patient had a past history of surgical treatment of the urinary tract. One case each of leiomyosarcoma involved the bladder and kidney and had been treated by partial cystectomy and total nephrectomy, respectively; there was no evidence of tumor recurrence at 2 and 3 years postoperatively. Tumor resection of the 2 rhabdomyosarcomas was impossible because of their extension into the surrounding organs. Biopsies were obtained from these tumors, and the patients were treated with chemotherapy. One of the patients died from the disease 2 years after diagnosis, and the other was alive at 2 years with the tumor.

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From the Pathology (Drs Watanabe, Hoshi, and Suzuki) and Urology (Dr Baba) Divisions, Fukushima Medical University School of Medicine Hospital, Fukushima City, Japan, and the Pathology Division, Jusendo General Hospital, Koriyama City, Japan (Dr Saito).

Reprints: Kazuo Watanabe, MD, Pathology Division, Fukushima Medical University Hospital, 1 Hikariga-oka, Fukushima City 960-1295, Japan (e-mail: w-kazuo@fmu.ac.jp).

Clinical Data and Results of Immunohistochemical Studies of Tumor Tissues*

Case	Age, y	Sex	Site	Initial Diagnosis	Size, mm	Therapy	Clinical Course	h-CD	Myogenin	Desmin	α -SMA	MSA
Pseudosarcomatous myofibroblastic tumor												
1	10	Male	Urinary bladder	Leiomyosarcoma	30	PCT	AWOD, 8 y	-	-	++	++	+++
2	38	Male	Urinary bladder	Leiomyoma	40	PCT	AWOD, 6 y	-	-	-	+++	+++
3	47	Female	Urinary bladder	Rhabdomyosarcoma	25	PCT, Chem	AWOD, 13 y	-	-	+++	-	+
Leiomyosarcoma												
4	69	Male	Urinary bladder	Leiomyosarcoma	52	PCT	AWOD, 2 y	+++	-	+++	+++	+++
5	73	Male	Kidney	Leiomyosarcoma	80	TNT	AWOD, 3 y	+++	-	+++	+++	+++
Rhabdomyosarcoma												
6	7	Male	Urinary bladder	Rhabdomyosarcoma	50	Chem	AWD, 2 y	-	+	++	+	+++
7	21	Male	Prostate	Rhabdomyosarcoma	Huge	Chem	DOD, 2 y	-	+++	+++	-	+++

* h-CD indicates high-molecular-weight caldesmon; α -SMA, α -smooth muscle actin; MSA, muscle-specific actin; PCT, partial cystectomy; chem, chemotherapy; TNT, total nephrectomy; AWOD, alive without disease; AWD, alive with disease; DOD, died of disease; -, negative; +, <25% positive cells; ++, 25% to 75% positive cells; and +++, >75% positive cells.

Histopathologic Features

The PMT lesions were composed of eosinophilic spindle cells arranged in weak fascicles with a partial herringbone pattern. The stroma of the tumors were diverse in each tumor, and myxoid material, collagenous fibers, and inflammatory cells (predominantly lymphocytes) were intermingled in varying degrees. The spindle cells in the tumors exhibited mild to moderate pleomorphism and nuclear atypia, but prominent atypia was not observed (Figure 1, A). The 2 leiomyosarcomas were of the conventional histologic type, and both rhabdomyosarcomas were of the embryonal type.

Immunohistochemical Features

The results of the immunohistochemical analyses are shown in the Table. One PMT (case 3) stained only focally for MSA, but the other 2 PMTs stained intensely for this marker. Two of 3 PMTs and both leiomyosarcomas stained intensely for α -SMA, but the rhabdomyosarcomas exhibited only focal positivity in one case. All but one of the PMTs stained intensely for desmin (Figure 1, B). In contrast, h-caldesmon was expressed only in leiomyosarcomas (Figure 2), and myogenin was expressed only in rhabdomyosarcomas (Figure 3).

COMMENT

Urogenital PMTs are uncommon lesions. Since the first report by Roth,¹ approximately 100 cases of PMT have been described in the English-language medical literature, including those of prostatic and renal origin.^{6,19} They are characterized by a sarcomatoid histology composed of myofibroblastic spindle cells variably arranged in fascicles, herringbone patterns, or storiform patterns, or having a feathery appearance with a myxoid or inflammatory stroma.¹⁻¹⁰ Most of the cases reported previously, as well as our cases of PMT, have been originally misdiagnosed as myogenic sarcomas.^{9,10} PMTs are benign lesions, and it is obviously important to distinguish them from malignant tumors to avoid unnecessary radical therapy.^{2,6,9,10,17} Because PMT of the urogenital tract is now well recognized, it can be diagnosed on the basis of clinical and light microscopic features. However, the diagnosis is at times still difficult when only small biopsy specimens are available. Leiomyosarcoma and rhabdomyosarcoma are the most problematic tumors in the differential diagnosis because

they overlap with PMT with respect to clinical features, including age of onset, tumor size and site, symptoms, and radiologic findings; these tumors also have similar cellular morphologies.^{20,21} In this study, we attempted to clarify which immunohistochemical characteristics are useful for this differential diagnosis by using antibodies to myogenin, h-caldesmon, desmin, α -SMA, and MSA.

Myogenin (Myf4) and MyoD1 are nuclear phosphoproteins that act as transcription factors, inducing muscle-specific gene expression by binding to regulatory sequences in their enhancer regions.^{22,23} Antibodies to these proteins can be used as sensitive and specific markers of rhabdomyosarcoma, and these antibodies do not react with cells of nodular fasciitis, leiomyomas, and inflammatory myofibroblastic tumors.²⁴⁻²⁷ Antimyogenin immunohistochemistry is extremely useful in this regard because it lacks the nonspecific cytoplasmic background staining that makes the interpretation of results of anti-MyoD1 immunohistochemistry difficult.²⁵⁻²⁷ In addition, h-caldesmon has also been recently identified as a marker of smooth muscle cells.^{18,28-32} Antibodies against h-caldesmon have been reported to stain cells of leiomyomas, leiomyosarcomas, and glomus tumors consistently but not cells of other mesenchymal lesions, such as nodular fasciitis, desmoid tumors, and solitary fibrous tumors in which actin or desmin immunoreactivities are frequently noted.^{18,30-32} Thus, h-caldesmon is thought to be a specific and sensitive marker for the diagnosis of smooth muscle tumors.

As expected on the basis of the findings of previous investigations,^{4,6,9,10,21,33} PMTs, leiomyosarcomas, and rhabdomyosarcomas all stained intensely for desmin and MSA. Antibodies against α -SMA also intensely stained the cells of PMTs and leiomyosarcomas and even focally stained the cells of rhabdomyosarcomas. Thus, desmin and actin are useful and sensitive markers for determining the myoid and myofibroblastic nature of the tumors but are not useful in differentiating between them. In contrast, myogenin showed extremely specific expression in rhabdomyosarcomas, and h-caldesmon showed extremely specific expression in leiomyosarcomas, whereas neither marker was expressed in PMTs. Hence, myogenin and h-caldesmon are useful in the differential diagnosis of urogenital myoid tumors. Although these immunohistochemical characteristics may not be present in poorly differentiated rhabdo-

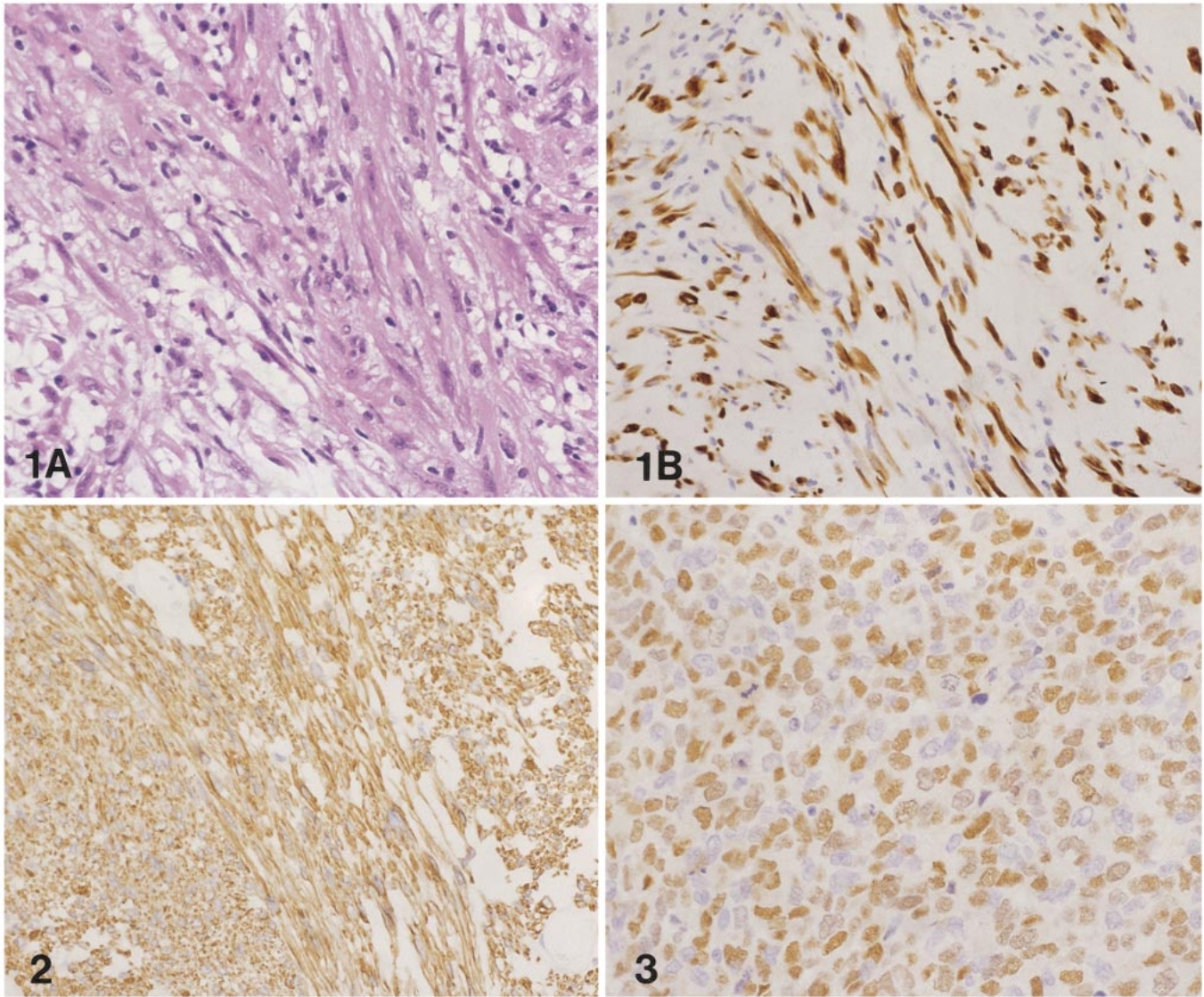


Figure 1. A, Pseudosarcomatous myofibroblastic tumor (case 3). The tumor is composed of spindle cells loosely arranged in fascicles with a myxoid stroma and inflammatory cells. The cells exhibit moderate pleomorphism and nuclear atypia (hematoxylin-eosin, original magnification $\times 200$). B, A large proportion of the tumor cells stain intensely for desmin (original magnification $\times 200$).

Figure 2. Leiomyosarcoma of the urinary bladder (case 4). The tumor shows diffuse immunoreactivity for high-molecular-weight caldesmon (original magnification $\times 200$).

Figure 3. Embryonal rhabdomyosarcoma of the prostate (case 7). The nuclei of many tumor cells are immunolabeled by an antibody to myogenin (Myf4) (original magnification $\times 400$).

myosarcomas and leiomyosarcomas,^{34,35} the prominent atypia and pleomorphism of these tumors should make it easy to distinguish them from PMTs. Certainly, sarcomatoid histology is one of the characteristics of inflammatory myofibroblastic tumors, but prominent atypia is uncommon in urogenital PMTs.

In summary, we determined the immunohistochemical profile of 7 urogenital myoid lesions including PMTs, leiomyosarcomas, and rhabdomyosarcomas. Reactivity for desmin and actin was noted to various degrees in all of these lesions, whereas h-caldesmon was expressed exclusively in leiomyosarcomas, and myogenin was expressed exclusively in rhabdomyosarcomas. We conclude that h-caldesmon and myogenin are extremely useful for

differentiating urogenital PMTs from other myoid lesions.

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