

## Case Report

# A case of primary spindle cell variant of embryonal rhabdomyosarcoma of the prostate

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**Abstract:** We treated a rare case of spindle cell variant of embryonal rhabdomyosarcoma (RMS) of the prostate of a patient referred to our hospital for gross hematuria. Computed tomography and magnetic resonance imaging revealed a 4-cm-diameter mass with focal cystic change. Transurethral resection (TUR) of the prostate was performed to diagnosis and treat for complete urinary retention. Microscopically, the TUR specimen almost comprised a fascicular proliferation of spindle-shaped tumor cells, leading to the diagnosis of spindle cell sarcoma. The consequent total prostatectomy revealed the presence of rhabdomyoblasts in addition to the spindle cell proliferation. A *MyoD1* p.L122R mutation was not detected in this tumor. The tumor recurred locally, with multiple metastatic lesions found soon after surgery. The patient received chemotherapy and radiation therapy but died 10 months after initial presentation. Although *MyoD1* mutation is reported to define a clinically aggressive subset of embryonal RMS, spindle cell variant of embryonal RMS shows extremely adverse clinical outcomes irrespective of *MyoD1* mutation.

**Keywords:** Prostate, spindle cell variant of rhabdomyosarcoma, synovial sarcoma, MyoD1

## Introduction

Rhabdomyosarcoma (RMS) is a mesenchymal tumor of myogenic differentiation and can be divided into three major variants with distinct histologic appearances: embryonal, alveolar, and pleomorphic. Alveolar RMS occurs on a specific chromosomal translocation, t(2;13)(q35;q14), or its variant, t(1;13)(p36;q14), resulting in the formation of a fusion gene, *PAX3-FKHR* or *PAX7-FKHR* [1]. On the contrary, a recurrent genetic alteration has not been identified in embryonal and pleomorphic RMS, except for recurrent *NCOA2* gene rearrangements in a small subset of spindle cell RMS occurring in infantiles or congenitally setting [2]. Recently, however, frequent and recurrent *MyoD1* homozygous p.L122R mutations have been identified as pathognomonic events in adult-type spindle cell RMS [3-5]. This mutation occurs in the conserved DNA-binding domain of *MyoD1* and leads to transactivation and MYC-like functions [5].

Spindle cell variant of embryonal RMS was first described in the pediatric population in 1992

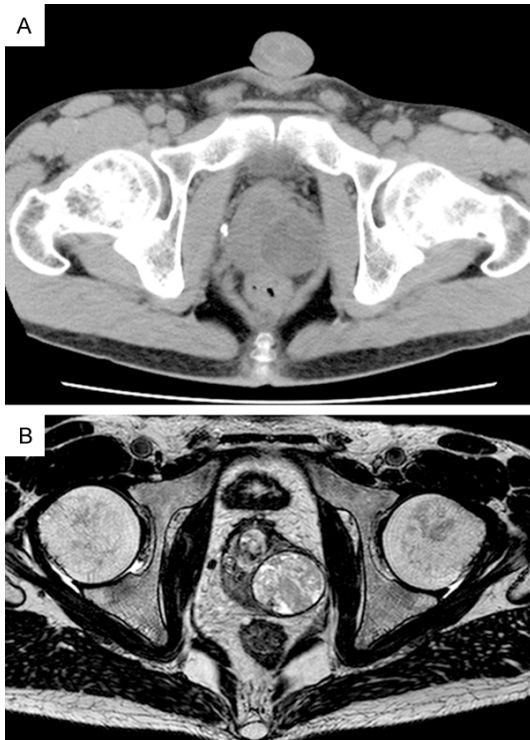
[6]. This rare variant occurs predominantly in the paratesticular region and has a better prognosis than the other subtypes of RMS [6]. In contrast to childhood spindle cell RMS, adult tumors have unfavorable prognosis because they exhibit a broader morphological spectrum, including sclerosing and pseudovascular types [5]. We report a rare case of spindle cell variant of embryonal RMS of the prostate.

## Case report

A 34-year-old man with gross hematuria was referred to our hospital. Laboratory test results were within the normal range except for mild anemia (hemoglobin 11.5 g/dL). Computed tomography and magnetic resonance imaging revealed a mass 4.0 cm in diameter with focal cystic change in the prostate (**Figure 1A** and **1B**). One month later, the patient complained of complete urinary retention.

For therapeutic and diagnostic purposes, transurethral resection (TUR) of the prostate was performed. Microscopically, the TUR specimen comprised a fascicular proliferation of spindle-

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**Figure 1.** A: Pelvic computed tomography scan shows a heterogeneously enhanced mass with focal cystic change in the prostate. The tumor margin is smooth. B: T2-weighted magnetic resonance imaging shows a mass with focal cystic change with heterogeneously high-signal-intensity. The mass is surrounded by a low-intensity fibrous capsule.

shaped tumor cells with round to oval nuclei (**Figure 2A**). Hypocellular areas of edematous stroma with massive necrosis were also noted. Because of the histology of the TUR specimen, the differential diagnosis was synovial sarcoma (SS). RNA was extracted from the TUR specimen, and reverse transcription polymerase chain reaction (RT-PCR) was performed to detect the SYT-SSX fusion transcript specific to SS. However, RT-PCR failed to detect an SYT-SSX fusion transcript (data not shown). As a result, the diagnosis was spindle cell sarcoma not other specified.

Radical transurethral prostatectomy with bilateral seminal vesiculectomy was promptly performed. Macroscopically, the tumor measured 4.0 x 3.2 x 2.0 cm, nearly consuming the left lobe of the prostate, and the cut surface of the resected tumor revealed an area of hemorrhagic necrosis (**Figure 2B**). Microscopically, the tumor histology resembled that of the TUR specimen except for significant numbers of

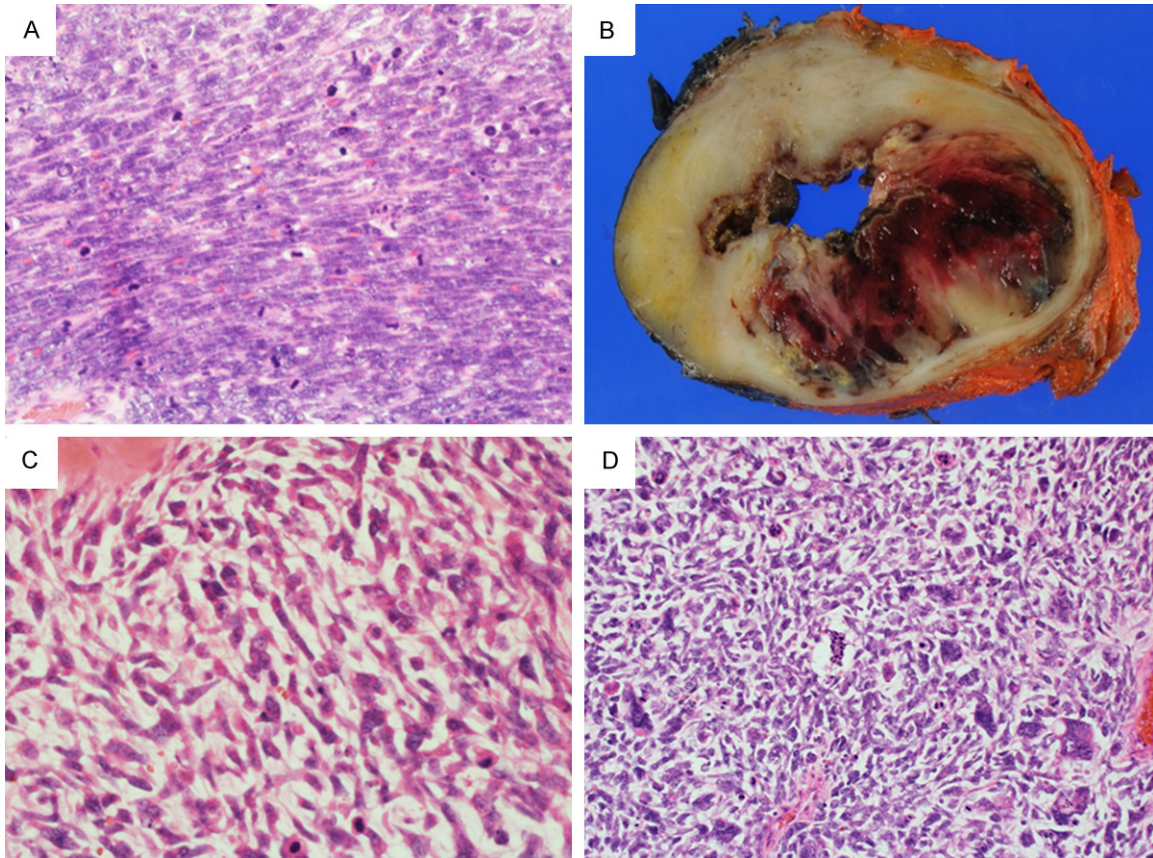
rhabdomyoblasts with elongated eosinophilic cytoplasmic tails known as tadpole cells or strap cells (**Figure 2C**). Cross-striations within the cytoplasm were not clearly observed. Immunohistochemical findings of the tumor cells were positive for vimentin, myoglobin, MIC2, muscle-specific actin, smooth muscle actin (SMA) and desmin and negative for keratin, CD34 (**Figure 3A-E**). The MIB-1 index was >90% (**Figure 3F**). Furthermore, genome DNA was extracted to assess the presence of the *MyoD1* mutation at codon 122, which has recently been identified as frequently mutated in aggressive RMS, including the spindle cell variant (3-5). However, an L122R homozygous mutation was not detected in this tumor (data not shown). On the basis of these findings, a final diagnosis of spindle cell variant of RMS was made. The peripheral resection margin did not show tumor, and both seminal vesicles were free of tumor cells. Neither vessel nor perineural invasion was seen.

Two months after the operation, three courses of neoadjuvant chemotherapy with vincristine, doxorubicin, and cyclophosphamide were administered to the patient for 2 months. During the treatment, he experienced severe back pain. The follow-up computed tomography scan revealed multiple metastases to the vertebrae and lungs as well as local recurrence. Irradiation of the thoracic vertebrae (total 24 Gy) and palliative radiation to bone metastatic lesions (8 Gy each) was performed. The patient was transferred to palliative care and died 10 months following the initial presentation.

### Discussion

Prostate sarcoma is an extremely rare and highly aggressive neoplasm responsible for <1% of primary prostate malignancies in adults [7, 8], although a variety of tumors have been reported, including RMS [7], leiomyosarcoma (LMS) [7], malignant peripheral nerve sheath tumor, Ewing sarcoma/primitive neuroectodermal tumor, fibrosarcoma [7], gastrointestinal stromal tumor [9, 10], and SS [7, 11, 12]. Prostate embryonal RMS is a common tumor in infants and children, with a median occurrence at age 5 years; however, it is rare in adults. Embryonal RMS in adults is characterized by a high degree of aggressive behavior, particularly the spindle cell variant. Because of predominant, but uniform spindle cell morphology in

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**Figure 2.** A: The specimen comprised spindle-shaped mesenchymal cells in fascicular fashion. Mitotic figures are frequently seen. B: The cut surface of the resected specimen shows central necrosis and bleeding. The whitish tumor had nearly consumed the prostate. C: Rhabdomyoblasts are scattered in some area. Rhabdomyoblasts have enlarged anaplastic nuclei with abundant eosinophilic cytoplasmic tail. D: Anaplastic tumor cells with hyperchromatic bizarre nuclei are scattered in some area.

the TUR specimen in this case, primary prostatic sarcoma, especially SS, was highly suspected. However, RT-PCR could not detect an SYT-SSX fusion transcript, which led to the diagnosis of spindle cell sarcoma not otherwise specified. The surgically resected tumor showed a variety of histological features in addition to the features of spindle cell sarcoma. Large atypical cells, including rhabdomyoblasts, comprised the striking feature that led to the final diagnosis of spindle cell variant of RMS.

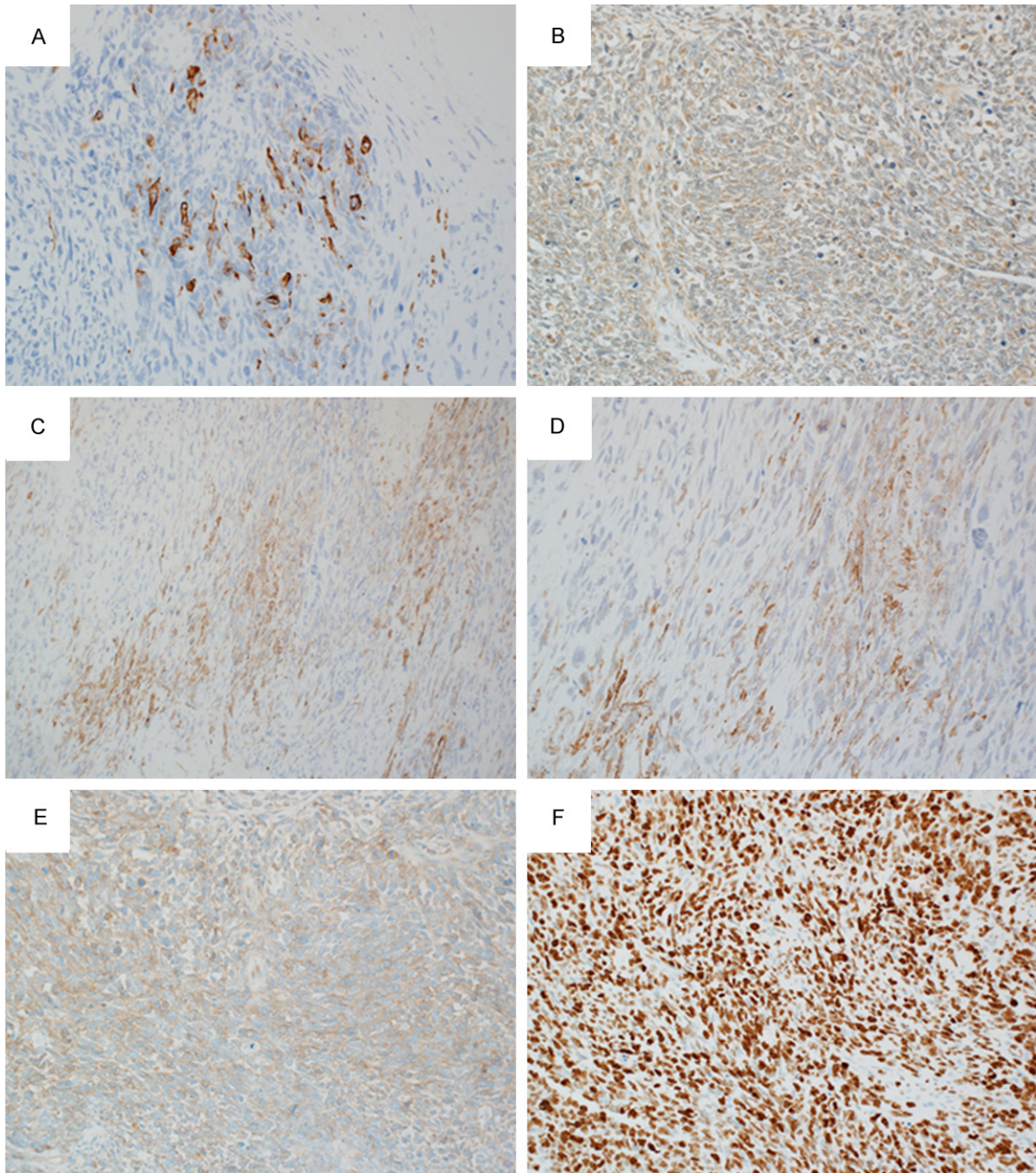
In the absence of typical rhabdomyoblasts, LMS should be considered as a differential diagnosis in addition to SS because, classically, spindle cell variant of RMS has been reported as leiomyomatous embryonal RMS [13], and LMS is the most frequently diagnosed sarcoma of the prostate [7]. Therefore, to further confirm the diagnosis, we assessed for the presence of

*MyoD1* mutation because recent reports have identified *MyoD1* as a driver mutation in aggressive RMS [3-5]. However, we could not confirm the presence of the *MyoD1* mutation in this patient, despite its reported frequency of approximately 40% [4, 5].

Immunohistochemically, spindle cell variant of RMS usually is positive for myogenic markers, such as desmin, myf-4, and HHF-35 (muscle-specific actin), but less common for fast myosin, myoglobin, and SMA [14]. The present case showed positive staining for desmin, myoglobin, SMA and HHF-35.

Spindle cell variant of RMS in adults is most common in the head and neck region and has a more aggressive phenotype compared with that in children [14]. To the best of our knowledge, this case is the second reported of spindle cell variant of RMS in the prostate [15]. The

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**Figure 3.** The tumor cells are positively stained for desmin (A), myoglobin (B), SMA (C), M-actin (D) and MIC2 (E). Scattered tumor cells have cytoplasmic tails strongly positive for desmin. Ki-67 labeling index is more than 90% (F).

patient in the previous case report died of disseminated disease 14 months after diagnosis [15], consistent with the present case. Multiple metastatic lesions formed in the present patient soon after surgery despite the negative resective margin and lymphatic/vessel invasion. Although the precise mechanisms are unclear, the dissemination of tumor cells into vessels during the radical TUR procedure might

have affected the formation of metastatic lesions.

We report a rare case of spindle cell variant of RMS in the prostate of an adult. This case did not carry a *MyoD1* mutation, which has recently been identified as a driver mutation in aggressive RMS. Although *MyoD1* mutation is reported to define a clinically aggressive subset of

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embryonal RMS, spindle cell variant of embryonal RMS shows extremely adverse clinical outcomes irrespective of *MyoD1* mutation.

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### Disclosure of conflict of interest

None.

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