Prostatic stromal sarcoma with neuroectodermal differentiation

Hitoshi Yamazaki1*, Teppei Ohyama2, Toshiki Tsuboi2, Yoshinori Taoka2, Dai Kohguchi2, Hiroyoshi Iguchi3 and Teruaki Ao2

Abstract: Prostatic stromal sarcoma is a fairly rare tumor that constitutes approximately 0.1–0.2% of all prostatic cancers. Detailed characteristics of the tumor are still unclear due to its rarity. We describe a case of prostatic stromal sarcoma in a 63 year-old man who suffered from urinary obstructive symptoms. Palliative transurethral resection was performed and the preliminary histopathological diagnosis was neuroendocrine carcinoma. After chemotherapy, total pelvic exenteration was performed. Histopathologically, the tumor was composed of monotonously proliferating small to medium-sized round cells, which existed in compact islands with loose or dense fibrovascular networks. Immunohistochemically, the tumor cells were widely positive for vimentin, CD56, CD99 and focally positive for synaptophysin, CD10, progesterone receptor, desmin and CD34, but negative for EMA, cytokeratin, estrogen receptor, S-100 and myoglobin. Most of the previously reported tumors exhibited positive stainability for CD10 and progesterone receptor. In addition to these markers, expressions of CD56, CD99 and synaptophysin were characteristically detected in our case. To the best of our knowledge, we present the first case of prostatic stromal sarcoma with characteristic immunohistochemical staining properties. Although the biological characteristics of this rare tumor have not yet been elucidated, these findings suggest prostatic stromal sarcoma can potentially show neuroectodermal differentiation.

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Keywords: Prostatic stromal sarcoma, STUMP, Immunohistochemistry, CD99, CD56, Synaptophysin, Neuroectodermal differentiation

Background
Prostatic stromal sarcoma (PSS) is a fairly rare tumor, constituting approximately 0.1% of all prostatic cancers [1,2]. Prostatic sarcoma and related proliferative lesions, including prostatic phyllodes tumors, have been classified as prostatic stromal tumors of uncertain malignant potential (STUMP) and prostatic stromal sarcoma (PSS) based on cellularity, mitotic index, cellular atypia and necrosis (WHO 2004) [3]. Some STUMP cases were reported as malignant transformation into PSS [4]. There has not yet been a clear differentiation between PSS and STUMP due to the rarity of these tumors. In this article, prostatic stromal sarcoma has potentially neuroectodermal characteristics.

Case presentation
The patient was a 63 year-old man who presented to the urologist with a one week history of dysuria, pollakiuria and an unrelieved feeling after urination. He had a previous history of diabetes mellitus and asymptomatic multiple brain infarction. He habitually drank alcohol and smoked and his mother died of gastric cancer. Abdominal ultrasonography revealed 343 ml of residual urine volume. Computed tomography revealed a prostatic mass lesion which protruded into the bladder space (Figure 1a). Gadolinium-enhanced T1 weighted magnetic resonance imaging also revealed the prostatic mass lesion had irregularly high signals (Figure 1b). Based on our clinical diagnosis of benign prostatic hypertrophy, palliative transurethral resection was performed. The specimen consisted of 20 grams of piecemealed prostate that was totally embedded in paraffin and histologically analyzed. Sections showed monotonously proliferating...
small to medium-sized round cells invading the edema-
tous stroma with coarseness and fineness and sparse or
dense patterns. The residual prostatic glands were iden-
tified. Immunohistochemically, the tumor cells were
positive for vimentin, CD56, synaptophysin (focal) but
negative for EMA, cytokeratin, S-100. The preliminary
histopathological diagnosis to decide the strategy for fur-
ther therapy was neuroendocrine carcinoma. He took
one series of chemotherapy, a combination of cisplatin
and irinotecan. Ten days after the last day of the chemo-
therapy, suprapubital radical cystprostatectomy with
rethrotectomy was performed. During the operation, the
urinary bladder could be detached from the rectum with
difficulty. Finally, low anterior rectal resection was add-
tionally performed, resulting in total pelvic exenteration.
When the urethra was cut, a part of the tumor was
pressed down from the urethral cavity. The gross fea-
tures of the tumor were elastic soft and translucently
whitish in color. After fixation in 10% formaldehyde the
prostate weighed 125 g and contained an ill-defined gray
whitish mass lesion, which focally exhibited necrosis
(Figure 2). The bladder and the retroperitoneal cavity
were diffusely infiltrated by the whitish tumor, which
was directly connected to the prostatic tumor. Although
the rectum was attached to the tumor mass, the rectal
dinghamyra was free from tumor invasion. The bladder
space was occupied by the tumor and narrowed, result-
ing in a slit-like space. Serial sections were analyzed and
revealed a round cell sarcomatous tumor with occasional
higher cellularity than that in the previous transurethine
resection. Tumor necrosis was occasionally identified.
The N/C ratio of the tumor cells was a relatively high
grade. Mitotic activity was measured as 12/10 HPF in
the higher cellularity area. The residual prostatic glands
were compressed to the periphery (Figure 3a). No lymph
nodal metastasis was observed. Immunohistochemically,
the tumor cells were widely positive for vimentin, CD56,
CD99 and focally positive for synaptophysin, CD10, pro-
gesterone receptor, desmin and CD34, but negative for
EMA, cytokeratin, estrogen receptor, S-100, GFAP and
myoglobin (Figure 3b,c,d). The Ki-67 index was about
70%. We finally diagnosed the tumor as prostatic stro-
mal sarcoma. Sixteen months later, the patient is alive
without local recurrence or distant metastasis.

Discussion
Prostatic stromal sarcoma is a rare tumor that constitu-
tes approximately 0.1–0.2% of all prostatic cancers [1,2].
Prostatic mesenchymal tumors sometimes cannot be clearly classified as histological entities due to their rar-
ity [5]. Except for prostatic mesenchymal tumors with
specialized differentiation, a histologically characteristic
classification involves prostatic stromal sarcoma and
prostatic stromal proliferation of uncertain malignant
potential (STUMP) [6-8]. These tumors have been
described on the basis of the histological similarity to
phyllodes tumors and have to be differentially diagnosed
as other specialized types of tumor, such as GIST, leio-
myosarcoma, rhabdomyosarcoma(RMS), and fibrosar-
coma [3]. RMS is the most common sarcoma of the
prostate, but is rarely reported in adult patients [9].
Prostatic stromal sarcoma and STUMP express female hormone receptors, especially progesterone receptor. These tumors seem to be derived from female hormone-dependent stromal cells [10]. Depending on the cellularity, mitosis and necrosis, these two tumors are histologically evaluated. An acceptable histological grading of stromal sarcoma has not yet been proposed due to the rarity of the tumor. Hasegawa reported that the ki-67 index was related to the prognosis of the tumor [4].

Recent immunohistochemical analysis revealed that both prostatic stromal sarcoma and STUMP usually express CD10, CD34 and the progesterone receptor [3,7,8,10-12]. This tumor sometimes positively reacts with smooth muscle actin. However, the detailed histopathological characteristics of the tumor cells have not yet been clearly elucidated. Kim reported a case of prostatic stromal sarcoma with rhabdoid features [13]. The tumor in our case was positive for CD56, CD99 (to our knowledge the second reported case) [14], synaptophysin and negative for EMA and cytokeratin. This is the first description of prostatic stromal sarcoma with immunohistochemically positive stainability for synaptophysin. There are other prostatic non-epithelial malignancies with potential neuroectodermal differentiation such as carcinosarcoma, ektomesenchymoma and primitive neuroectodermal tumor (PNET), which have to be distinguished from our case of prostatic stromal sarcoma. Patient age is a useful marker for differential diagnosis, although PNET and malignant ektomesenchymoma are rarely reported in young adult prostate cancer patients [15-18]. Most PNET cases reveal positive immunoreactivity for CD99, but are negative for progesterone receptor. Carcinosarcoma contains elements of epithelial malignancy which exhibit some types of cytokeratins.

PSS is suspiciously derived from mesenchymal pluripotent stem cells in the prostatic stroma. As few cases of STUMP change to PSS in the history, some genetic transformations are considered to be related to PSS [4,19]. Arva showed that some cases of prostatic squamous cell carcinoma were derived from hormonal or radiation-treated prostatic adenocarcinoma [20]. Unexpected irradiation may be one of the risk factors of PSS [21,22]. Babarović reported a case of high grade angiosarcoma arising in fibroadenoma and suggested the possibility that severe inflammatory reaction, for example silicon granuloma, may cause malignant transformation of stromal cells in the affected area [23,24]. These factors may give rise to an exuberant stromal response and cause some genetic events in the mesenchymal pluripotent stem cells. We could classify PSS as two categories, which are de novo tumorigenesis and malignant transformation step by step [20]. However, there are no

Figure 3 Microscopic findings. a) The tumor was made up of sarcomatoid oval to spindle cells. (HE x 100) b) Immunostaining with CD56 showed positive results for tumor cells on the cell membrane (CD56 x 200). c) Immunostaining with synaptophysin focally showed positive results for the tumor cells in the cytoplasm (synaptophysin x 200). d) Immunostaining with CD99 showed positive results for tumor cells on the cell membrane (CD99 x 200).
authentic molecules which directly cause prostatic stromal tumorigenesis. Fibroblast growth factor 8 (FGF8),
the eighth member of the fibroblast growth factor family contains alternatively spliced mRNA isoforms.
Fibroblast growth factor 8b(FGF8b) is an androgen-induced growth factor with potent oncogenic activity [25-27].
Elo reported the results of prostate-targeted fibroblast growth factor 8b transgenic mice [28]. These mice
showed progressive changes in prostatic stroma, as well as the prostatic epithelium. Furthermore, FGF8b is
the predominant FGF8 spliceform necessary for proper posterior neural formation in Xenopus [29]. Amsterdam
reported the relationship between fgf8 misregulation and neuronal tumors in Zebrafish [30]. This knowledge
suggests FGF8b is related to potential neuroectodermal differentiation in prostatic stromal tumorigenesis. Some
hormonal imbalances, including androgen imbalance, may cause prostatic stromal progression, which could
lead to prostatic stromal neoplasia. We hereby point out that PSS may also possess neuroectodermal characteristics.

Conclusions
We describe a rare case of prostatic stromal sarcoma (PSS) presenting with characteristic immunohistochemical
staining properties. To our knowledge, this case is the first case of PSS with positive stainability for synap-
tophysin, as well as CD99 and CD56.

Consent
Written informed consent was obtained from the patient for publication of this case report and accompanying
images. A copy of the written consent is available for review by the Editor-in-Chief of Diagnostic Pathology.

Competing interests
We do not have any competing interests for our manuscript.

Authors’ contribution
HY was responsible for data collection and drafted the manuscript. TC, TT, YT, OK and TA made contributions to acquisition of clinical data and performed surgical procedure. HL performed radiological interpretation and performed surgical procedure. HY was responsible for data collection and drafted the manuscript. TO, TT, DK and TA made contributions to acquisition of clinical data and as well as the prostatic epithelium.

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