Urologia Internationalis

Original Paper

Urol Int 2021;105:206–214
DOI: 10.1159/000508763

Received: February 17, 2020
Accepted: May 16, 2020
Published online: November 20, 2020

Clinical and Pathological Features of Prostatic Stromal Tumor of Uncertain Malignant Potential: A Retrospective Study of 23 Chinese Cases

Qi Shen[a, b] Zhaohui Zhou[a] Zhenhua Liu[a] Shuai Hu[a, b] Zhiyong Lin[c] Shaobo Li[d] Senmao Li[a] Hualin Song[a] Yuke Chen[a] Yisen Meng[a] Yu Wang[a] Yu Fan[a] Xin Li[a] Yunxiang Xiao[a] Qun He[a, b] Jie Jin[a] Qian Zhang[a] Wei Yu[a]

[a]Department of Urology, Peking University First Hospital, Institute of Urology, Peking University, National Research Center for Genitourinary Oncology, Beijing, China; [b]Department of Urological Pathology, Peking University First Hospital, Institute of Urology, Peking University, National Research Center for Genitourinary Oncology, Beijing, China; [c]Department of Radiology, Peking University First Hospital, Beijing, China; [d]School of Basic Medicine, Fudan University, Shanghai, China

Keywords
Prostate · Hyperplasia · Stromal tumor of uncertain malignant potential · Prognosis

Abstract
Introduction: Prostatic stromal tumor of uncertain malignant potential (STUMP) is a rare disease that may coexist with prostate stromal sarcoma (PSS). We aimed to analyze the histological and clinical features of STUMP. ***Methods:*** Twenty-three patients diagnosed with STUMP from 2008 to 2019 were included. Clinicopathological and follow-up information was collected. In the subgroup analysis, we divided the patients into a pure STUMP group (N = 18) and a mixed STUMP (STUMP coexisting with PSS) group (N = 5). Student's t test was used to compare the 2 groups. ***Results:*** Patients had a mean age of 55.5 ± 19.4 years and an average follow-up time of 42.3 months. The mean prostate volume was 109.2 ± 73.5 cm^3, and the mean prostate-specific antigen was 8.03 ± 10.5 ng/mL. In the subgroup analysis, 16.7% (2/12) of pure STUMP patients had disease progression, while 100% (3/3) of mixed STUMP patients suffered from recurrence. Compared with the pure STUMP group, the mixed STUMP group was younger (37.2 vs. 60.6 years, $p = 0.013$) and had lower expression of estrogen receptor and progesterone receptor ($p = 0.004$ and $p < 0.001$, respectively). ***Conclusion:*** STUMP is a rare disease with a relatively good prognosis. However, there is still a possibility of disease progression or coexistence with stromal sarcoma. Timely diagnosis and regular monitoring may be helpful in improving treatment outcomes.

Introduction

Malignant tumors from the stroma, as opposed to prostate adenocarcinomas, only account for 0.1–0.2% of all prostate malignancies [1]. Gaudin et al. [2] first classi-

Qi Shen, Zhaohui Zhou, and Zhenhua Liu contributed equally to this work.

karger@karger.com
www.karger.com/uin

Qian Zhang or Wei Yu
Department of Urology, National Urological Cancer Center
Peking University First Hospital and Institute of Urology, Peking University
8 Xishiku Street, Xicheng Dist, Beijing 100034 (China)
zhangqianbmu@vip.sina.com or yuweif@126.com

Table 1. Clinical characteristics of STUMP patients

Patient No.	Age, years	Diagnostic specimen	Hematuria	Hemato-spermia	LUTS	Urinary retention	Oral medication[a]	DRE	tPSA, ng/mL	*f*/*t* ratio	Prostate volume, mL[b]
1	27	TURP	Yes	No	Yes	Yes	No	Prostatic enlargement	8.05	0.16	70.0
2	31	Needle biopsy	No	No	Yes	No	No	Prostatic enlargement	48.10	0.06	94.0
3	73	TURP	No	No	Yes	Yes	No	Prostatic enlargement	4.42	0.33	142.0
4	67	Needle biopsy	No	No	Yes	Yes	Yes	Prostatic enlargement	8.49	0.15	97.4
5	66	RP	Yes	No	Yes	Yes	No	/	2.02	0.22	55.0
6	77	Needle biopsy	Yes	No	Yes	No	Yes	Prostatic enlargement	3.80	0.20	236.2
7	66	RP	Yes	No	Yes	No	Yes	Prostatic enlargement	13.30	0.09	184.0
8	73	TURP	No	No	Yes	Yes	No	Prostatic enlargement	2.63	0.26	55.0
9	81	TURP	No	No	Yes	Yes	No	Prostatic enlargement	9.50	0.08	48.0
10	71	TURP	No	No	Yes	No	No	Prostatic enlargement	7.40	0.08	37.1
11	71	Needle biopsy	No	No	Yes	Yes	Yes	Prostatic enlargement	18.10	0.08	119.0
12	51	RP	No	No	No	No	No	Prostatic enlargement	1.69	0.21	158.4
13	39	Needle biopsy	No	No	Yes	Yes	No	Prostatic enlargement and nodules	1.78	0.14	20.6
14	78	RP	No	No	Yes	No	No	Prostatic enlargement	8.90	0.26	175.0
15	58	Needle biopsy	No	No	Yes	Yes	No	Prostatic enlargement and nodules	6.87	0.05	77.0
16	53	RP	No	No	No	No	No	Prostatic enlargement	24.00	/	72.0
17	75	TURP	No	No	Yes	No	No	Prostatic enlargement	3.47	0.15	89.0
18	33	Needle biopsy	No	No	Yes	Yes	No	Prostatic enlargement and nodules	1.08	0.35	46.0
19	37	RP	Yes	No	Yes	No	No	Prostatic enlargement	0.70	0.10	102.0
20	25	Needle biopsy	No	No	Yes	Yes	No	Prostatic enlargement	1.15	0.12	346.0
21	61	RP	Yes	No	No	No	No	Prostatic enlargement	5.6	0.17	93.0
22	40	TURP	No	No	Yes	Yes	No	Prostatic enlargement	0.78	0.08	74.0
23	23	TURP	No	No	Yes	Yes	No	Prostatic enlargement	2.75	0.09	121.2

Patient Nos. 1–18 (N = 18): pure STUMP group; patient Nos. 19–23 (N = 5): mixed STUMP (STUMP coexisting with PSS) group. DRE, digital rectal examination; LUTS, lower urinary tract symptoms; No., number; PSA, prostate-specific antigen; PSS, prostate stromal sarcoma; RP, radical prostatectomy; STUMP, stromal tumor with uncertain malignant potential; /, no data. [a] Have a history of 5-α-reductase inhibitors. [b] Calculated by B-ultrasound.

fied prostate stromal tumors into 2 types: prostate stromal sarcoma (PSS) and prostatic stromal tumor of uncertain malignant potential (STUMP). Mokhtari et al. [3] found that the prevalence of STUMP in patients diagnosed with benign prostate hyperplasia was 0.43%. STUMP can be further divided into 4 groups according to the following features: degenerative atypia, hypercellular spindle cells, myxoid spindle cells, and phyllode-like patterns [4].

Even with the low incidence of STUMP, its characteristics still need further study. We asked the following questions: what are the clinicopathological characteristics of STUMP in Chinese patients? When PSS coexists in STUMP samples, are there any differences in the characteristics compared with those of pure STUMP? We retrospectively analyzed the histological and clinical features of 23 STUMP patients from our center, hoping to further elaborate on the diagnosis and treatment of STUMP.

Table 2. Clinicopathological features of STUMP patients and comparison between the 2 subgroups (pure vs. mixed STUMP group)

	Total (N = 23)	Pure STUMP (N = 18)	Mixed STUMP (STUMP coexisting with PSS, N = 5)	p value
Age, years	55.48±19.39	60.56±17.50	37.20±15.21	**0.013***
PSA, ng/mL	8.03±10.50	9.64±11.36	2.20±2.07	0.166
f/*t* ratio	0.16±0.09 (N = 22)	0.17±0.09 (N = 17)	0.11±0.04	0.054
Volume, cm^3	109.21±73.49	98.64±58.93	147.24±112.40	0.198
Ki-67 positive rate (%)	10.67±14.61 (N = 12)	5.63±5.98 (N = 8)	20.75±22.26 (N = 4)	0.268
ER score	1.27±1.27 (N = 12)	1.75±1.17 (N = 8)	0 (N = 4)	**0.004***
Vim score	4.09±1.04 (N = 11)	4.14±1.07 (N = 7)	4.00±1.16 (N = 4)	0.840
SMA score	2.57±1.51 (N = 14)	2.90±1.60 (N = 10)	1.75±0.96 (N = 4)	0.208
CD34 score	2.29±1.31 (N = 17)	2.33±1.37 (N = 12)	2.20±1.30	0.856
Actin score	2.38±1.69 (N = 8)	2.00±1.41 (N = 4)	2.75±2.06 (N = 4)	0.570
PR score	2.00±1.78 (N = 13)	3.25±0.87 (N = 8)	0	**<0.001***

Student's t test was used to compare the 2 groups (mean value). Scoring standards: (−): 0; (+/−): 1; (partial +): 2; (+): 3; (++): 4; and (+++): 5. * $p < 0.05$. ER, estrogen receptor; PR, progesterone receptor; PSS, prostate stromal sarcoma; SMA, smooth muscle actin; STUMP, stromal tumor with uncertain malignant potential; Vim, vimentin; PSA, prostate-specific antigen.

Materials and Methods

Patient Selection

A total of 23 cases diagnosed as STUMP by prostate biopsy, transurethral resection of the prostate (TURP), or radical prostatectomy (RP) from 2008 to 2019 in our center were included in this study. All patients provided informed consent. Clinicopathological and follow-up information was collected. Patients were excluded from the analysis if they had (1) malignant tumors in other organs, (2) unclear diagnosis, or (3) unavailable specimens. The research was approved by the Ethics Committee of our hospital. Informed consent was obtained from all individual participants included in the study.

Specimen Processing and Diagnosis

All specimens were obtained from the Pathology Department of our center. The specimens were formalin-fixed, dehydrated, paraffin-embedded, and sliced (5 μm thick). Histological features of each tumor were identified by staining the most distinct sites of the tumor with hematoxylin-eosin (H&E) and immunohistochemical (IHC) staining (for antibody information, see online suppl. Table 1 at www.karger.com/doi/10.1159/000508763; Abcam, USA; CST, USA). Two experienced pathologists independently described the pathological features of the section. When a discrepancy occurred, a third pathologist examined the slides and determined the final diagnosis. We divided the expression of indicators into 6 levels: (−), (+/−), (partial +), (+), (++), and (+++). For the convenience of statistics, we converted the degree of expression into scores (scoring standards: [−]: 0; [+/−]: 1; [partial +]: 2; [+]: 3; [++]: 4; and [+++]: 5).

Statistical Analysis

STUMP could also coexist with PSS in some patients. In the subgroup analysis, we divided the total patients into a pure STUMP group (N = 18) and a mixed STUMP (STUMP coexisting with PSS at the time of diagnosis or subsequent treatment) group (N = 5) [5]. We used SPSS v22.0 software (IBM Corp., Armonk, NY, USA) for statistical description and analysis. Student's t test was used to compare groups, and Fisher's test was used to determine differences. All reported p values are 2-sided, and $p < 0.05$ was considered statistically significant.

Results

Clinical Features

STUMP patients had a mean age of 55.5 ± 19.4 (range: 23–81) years, and most of them had symptoms related to urination, such as difficulty urinating and frequent urination. Approximately one quarter (6/23) of the patients developed hematuria. Of these 23 patients, 4 (17.4%) had constipation and 13 (56.5%) had urinary retention. In total, 4 (17.4%) patients were given a 5α-reductase inhibitor and 3 (13.0%) were given an α-receptor blocker, but the effects were moderate. From the digital rectal examination results, we found that the majority of patients had enlarged prostates. In 3 patients, nodules were palpable. The mean prostate volume was 109.2 ± 73.5 (range: 20.6–346.0) cm^3, and the mean prostate-specific antigen (PSA) was 8.03 ± 10.5 (range: 0.7–48.1) ng/mL (Table 1). Patients were followed up for an average of 42.3 (range: 6–86) months.

In the subgroup analysis, compared with the pure STUMP group, the mixed STUMP group was younger (37.2 ± 15.2 vs. 60.6 ± 17.5 years, p = 0.013) and tended to have a lower *f*/t ratio in PSA (p = 0.054). Although there was no significant difference, we found the mean PSA lev-

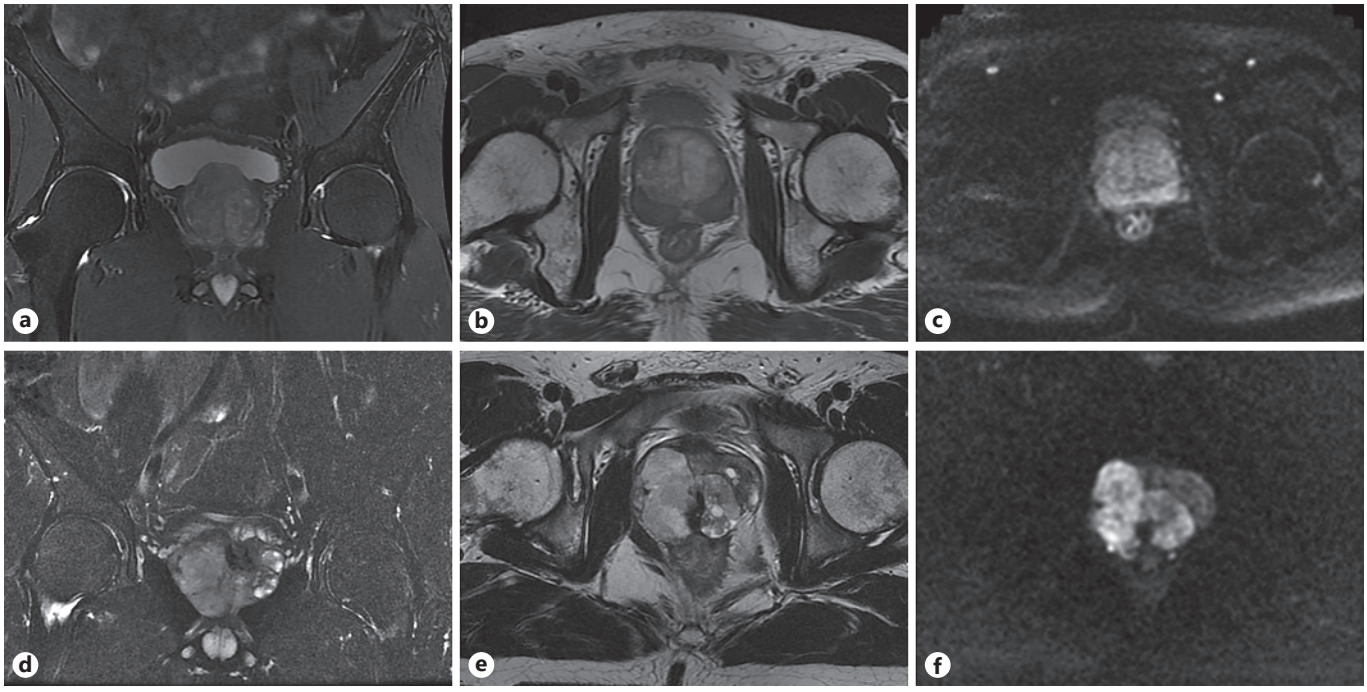


Fig. 1. Examples of MRI data of STUMP in 2 subgroups (pure STUMP and mixed STUMP). Both groups showed increased prostate volume. (1) Example of pure STUMP. The nodules showed low T2WI signal, and no significant increase in DWI was observed (patient No. 4 in Table 1). T2-weighted image on coronal slice (**a**); T2-weighted image on transverse slice (**b**); diffusion image (DWI) (**c**). (2) Example of mixed STUMP (STUMP coexisted with PSS). The tumor presented a mixture of high and low T2WI signals along with high DWI signal, and the enhancement scan showed uneven enhancement, and the prostate capsule is not continuous (patient No. 19 in Table 1). T2-weighted image on coronal slice (**d**); T2-weighted image on transverse slice (**e**); diffusion image (DWI) (**f**). MRI, magnetic resonance imaging; STUMP, stromal tumor with uncertain malignant potential; PSS, prostate stromal sarcoma.

el of the mixed STUMP group was in the normal range (2.2 ± 2.1 ng/mL), while the mean prostate volume reached 147.2 ± 112.4 cm^3 (pure STUMP group: mean PSA: 9.6 ± 11.4 ng/mL; mean prostate volume: 98.6 ± 58.9 cm^3) (Table 2). In a representative comparison of magnetic resonance imaging results of the 2 groups, both groups showed increased prostate volume. In patients with pure STUMP, the nodules showed a low T2WI signal, and no significant increase in DWI was observed. However, in the mixed STUMP group, the tumor presented a mixture of high and low T2WI signals along with high DWI signal, and the enhancement scan showed uneven enhancement and the prostate capsule was not continuous (Fig. 1).

Pathological Features

In most H&E slices, the stromal cells showed significant proliferation, large nuclei, atypia, and extensive or localized inflammatory cell infiltration. In IHC staining, because different patients have their own morphological features, in addition to the commonly used indicators, such as vimentin (Vim), CD34, smooth muscle actin (SMA), progesterone receptor (PR), estrogen receptor (ER) and Ki-67, we used different antibodies as a differential diagnosis method. For example, we used Bcl-2, S-100, actin, etc., as indicators to identify fibroma; we added desmin and other indicators to identify SCC; and we added NSE, S-100, and other indicators to identify neurogenic tumors. After statistical analysis, we found that among all the indicators, Vim (100%), Ki-67 (84.6%), actin (75.0%), SMA (78.6%), AR (50.0%), CD34 (64.7%), ER (54.5%), and PR (56.3%) had a positive rate of >40% (indicators with count >4 were included) (Tables 3, 4).

In the subgroup analysis, compared with the pure STUMP group, the mixed STUMP group had disordered cell arrangement and a lower expression rate of ER and PR ($p = 0.004$ and $p < 0.001$, respectively). Although there was no significant difference, the mean Ki-67 positive rate in the mixed STUMP group was higher (20.75 ± 22.26%) than that in the pure STUMP group (5.63 ± 6.0%) (Table 2; Fig. 2).

Table 3. Pathological characteristics of STUMP patients (IHC examination, part 1)[a]

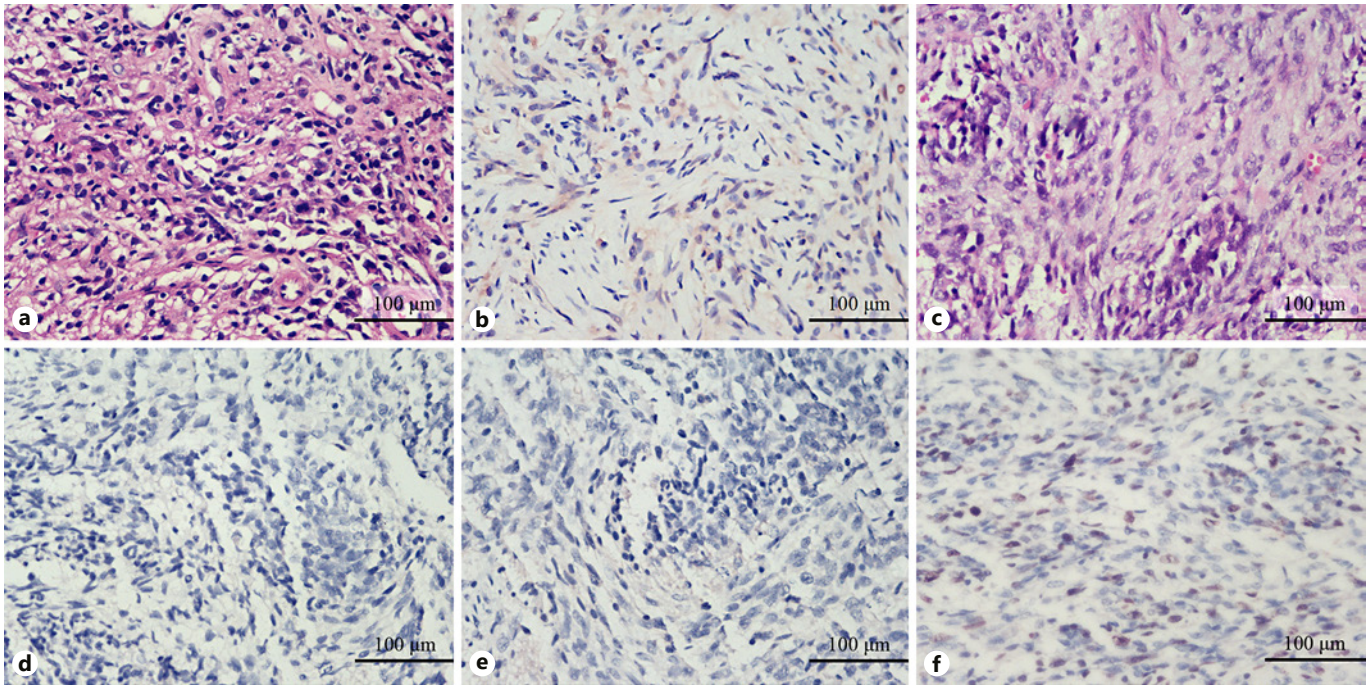
Patient No.	Age, years	Diagnostic specimen	Vim	SMA	CD34	AR	ER	Ki-67	Actin	PR	CD68	PSA	PsAP
1	27	TURP	(+++)	(+++)	(+)	(−)	/	(+<1%)	/	/	/	/	/
2	31	Needle biopsy	/	(Partial +)	(+)	/	(Partial +)	(+<3%)	(Partial +)	(Partial +)	/	/	/
4	67	Needle biopsy	(+++)	(+)	(+/−)	/	/	/	/	(Partial +)	(+)	(−)	(−)
5	66	RP	(+)	(−)	(+)	/	(−)	(+10%)	(−)	(+)	/	/	/
7	66	RP	(+++)	(++)	(+/−)[b]	(+)	(−)	(+20%)[b]	/	(−)	/	/	/
10	71	TURP	/	(+)	(+)	/	(Partial +)	(+5%)	(+)	(+)	/	/	/
11	71	Needle biopsy	/	(+)	(−)	/	/	(+3%)	/	(−)	/	(−)	/
12	51	RP	(+)	(+)	(+)	/	(Partial +)	/	/	(+)	/	/	/
13	39	Needle biopsy	(+)	/	(−)	/	(+)	(+<5%)	/	(+)	/	(−)	/
14	58	Needle biopsy	/	(+++)	(+)	(+)	/	/	/	(++)	/	/	/
16	53	RP	/	/	(Partial +)	/	(Partial +)	(+3%)	(+)	(+)	/	/	/
17	33	Needle biopsy	(+++)	(+/−)	(+++)	/	(+)	(+5%)	/	(+++)	/	/	/
19	37	RP	/	/	(+/−)	/	(−)	(+40%)	(+++)	(−)	/	(−)	/
20	25	Needle biopsy	(+++)	(+/−)	(+)	/	/	/	/	(−)	/	/	/
21	61	RP	(+++)	(+)	(++)	/	(−)	(−)	(−)	(−)	/	(−)	/
22	40	TURP	(+)	(Partial +)	(Partial +)	(−)	(−)	(+40%)	(+)	(−)	/	/	/
23	23	TURP	(+)	(+)	(+/−)	/	/	(+<3%)	(+)	(−)	/	/	/

Patient Nos. 1–18 ($N = 18$): pure STUMP group; patients Nos. 19–23 ($N = 5$): mixed STUMP (STUMP coexisting with PSS) group. CD34, cluster of differentiation 34; ER, estrogen receptor; PR, progesterone receptor; PSA, prostate-specific antigen; PSS, prostate stromal sarcoma; RP, radical prostatectomy; SMA, smooth muscle actin; STUMP, stromal tumor with uncertain malignant potential; Vim, vimentin; IHC, immunohistochemical; /, no data. [a] Patient Nos. 3, 6, 8, 9, 15, and 18 did not receive IHC examination. [b] Needle biopsy results (1 month before prostatectomy) of patient No. 8: CD34 (+++), Ki-67 (+1%).

Treatment and Follow-Up

Among the 23 patients admitted to our hospital and diagnosed with STUMP, 8 were diagnosed by needle biopsy and 15 were diagnosed by surgery (TURP [$N = 9$] and RP [$N = 6$]). We performed a follow-up study with these patients. Of the 8 patients who received needle biopsy, 2 were under surveillance and 4 underwent surgery (TURP [$N = 2$] and prostatectomy [$N = 2$]) (2 were lost to follow-up). Nine patients received TURP, and they received treatment such as surveillance ($N = 3$) and surgery (re-TURP [$N = 2$] and radical cystectomy [$N = 2$]) (2 were lost to follow-up). Other patients ($N = 6$) received prostatectomy followed by surveillance ($N = 3$, and 2 patients had recurrence), or total pelvic exenteration ($N = 1$) (2 were lost to follow-up) (Table 5).

In the subgroup analysis of patients who had followed up, 16.7% (2/12) of pure STUMP patients had disease progression, while 100% (3/3) of mixed STUMP patients suffered from recurrence. The main form of progression in pure STUMP patients was progressive dysuria, which occurred in 0.5–2 years. For the first patient (No. 17 in Table 1), prostate hyperplasia was found 6 months after TURP, and he was then given maintenance therapy with α-receptor blockers. Although there was no urine retention for approximately 7 years, the urination situation is not very satisfactory. The other patient (No. 1 in Table 1) underwent TURP again 2 years after the first operation due to dysuria (70 mL prostate volume in the first hospitalization and 190 mL prostate volume in the second hospitalization) and developed dysuria again 5 years later (no oral medicine was used). For the mixed STUMP group, the time of recurrence was 0.5–1 year. The first patient relapsed 6 months after RP and died 1 year later. The second patient underwent total pelvic exenteration due to



Color version available online

Fig. 2. Pathological images of STUMP (H&E staining, ×400. IHC staining, ×400). (1) Example of pure STUMP (patient No. 4 in Table 1). Dense arrangement of STUMP cells was observed in H&E staining, and positive PR staining was shown in IHC staining. H&E staining (**a**); PR staining (positive staining) (**b**). (2) Example of mixed STUMP (STUMP coexisted with PSS) (patient No. 19 in Table 1). H&E staining showed mixed cells with disordered arrangement, varying in size and shape from cell to cell. IHC staining showed negative ER/PR staining and positive Ki-67 staining. H&E staining (**c**); PR staining (negative staining) (**d**); ER staining (negative staining) (**e**); Ki-67 staining (positive staining) (**f**). STUMP, stromal tumor with uncertain malignant potential; IHC, immunohistochemical; H&E, hematoxylin-eosin; PSS, prostate stromal sarcoma.

recurrent and rectal invasion 6 months after RP. The third patient relapsed 1 year after TURP and underwent radical cystectomy (concurrent prostatectomy).

Discussion

STUMP is a tumor originating from the prostate stroma. The age of STUMP onset has been reported in the literature as ranging from 27 to 83 years, with a median patient age of 58 years [6]. STUMP has no specific clinical manifestations, and the characteristics are mainly progressive lower urinary tract symptoms, such as dysuria, acute urinary retention, hematuria, urinary frequency, and other changes in urination.

For patients with no or slight elevation of PSA, a rapid increase in prostate volume, and hard nodes in the prostate (found by digital rectal examination), the possibility of STUMP should be considered. Magnetic resonance imaging can provide information about the location and extent of tumor invasion. However, the final diagnosis of STUMP still depends on pathological evidence, and B-ultrasound-guided transrectal prostate biopsy is a reliable method for diagnosis. The main histological features of STUMP are atypical and specific proliferation of prostatic interstitial cells. In the IHC staining analysis, tumor cells expressed CD117, CD34, Vim, desmin, PR, and SMA [7]. It should be noted that the absence of sarcomas in prostate biopsy does not guarantee the stability of the STUMP [8].

STUMP is generally considered to be a neoplastic lesion with a morphology similar to that of PSS [7]. Although most of the STUMP cases are benign and androgen-dependent lesions, some of them can progress to PSS [9]. Pan et al. [10] showed that prostate interstitial tumors share common chromosomal imbalances (including chromosome 13 and 14 deletions), and the tumor mutation burden of STUMP and low-grade stromal sarcoma is lower than that of high-grade sarcoma. Differential diagnosis of STUMP and PSS mainly depends on histopathological manifestations and IHC markers. In patients with PSS, staining for myogenic antibodies, such as SMA,

Table 4. Pathological characteristics of STUMP patients (IHC examination, part 2)[a]

Patient No.	Age, years	Diagnostic specimen	CK8/18	AE1/AE3	LCA	Des	NSE	CA-9	CD99	bcl-2	CD117	S-100	M630	CK5/6	P504S (–)
1	27	TURP	/	/	/	/	/	/	/	/	/	/	/	/	/
2	31	Needle biopsy	/	/	/	/	/	/	/	/	/	/	(+)	/	/
4	67	Needle biopsy	(–)	(–)	(++)	/	/	/	/	/	/	/	/	/	/
5	66	RP	/	(–)	/	(–)	(+/–)	/	/	/	/	/	/	/	/
7	66	RP	/	/	/	/	/	/	/	/	/	/	(++)	(++)	(+)
10	71	TURP	/	/	(Partial +)	(+)	/	/	/	/	/	/	/	/	/
11	71	Needle biopsy	/	(–)	/	/	/	/	/	/	/	/	/	/	/
12	51	RP	/	(–)	/	(+)	/	(Partial +)	/	(+)	/	/	/	/	/
13	39	Needle biopsy	/	(–)	/	/	(–)	/	/	(+)	(–)	/	/	/	/
14	58	Needle biopsy	/	/	/	/	/	/	/	/	(–)	(–)	/	/	/
16	53	RP	/	/	/	/	/	/	/	/	/	/	(+)	(+)	(–)
17	33	Needle biopsy	/	(–)	/	/	/	/	/	/	/	/	/	/	(–)
19	37	RP	/	(–)	/	/	/	/	/	/	/	/	/	/	/
20	25	Needle biopsy	/	/	(–)	(–)	(+/–)	/	/	/	/	/	/	/	/
21	61	RP	/	/	/	(–)	/	/	/	/	/	/	/	/	/
22	40	TURP	/	(–)	/	/	(Partial +)	/	(Weak +)	(Partial +)	(–)	(Partial +)	/	/	/
23	23	TURP	/	/	/	/	/	/	/	/	/	/	/	/	/

Patient Nos. 1–18 ($N = 18$): pure STUMP group; patient Nos. 19–23 ($N = 5$): mixed STUMP (STUMP coexisting with PSS) group. AE1/AE3, pan-cytokeratin; Bcl-2, B-cell lymphoma-2; CA-9, carbonic anhydrase 9; CD99, cluster of differentiation 99; CD117, cluster of differentiation 117; CK8/18, cytokeratin 8/18; Des, desmin; LCA, leukocyte common antigen; NSE, neuron-specific enolase; P504S, α-methylacyl coenzyme A racemase; S-100, S-100 protein; RP, radical prostatectomy; STUMP, stromal tumor with uncertain malignant potential; IHC, immunohistochemical; /, no data. [a] Patient Nos. 3,6, 8, 9, 15, and 18 did not receive IHC examination.

desmin, muscle, and MyoD1, was positive [11, 12]. Other parameters, such as cellular characteristics, mitotic activity, necrosis, and expansion into the surrounding organs, can also be used to distinguish the 2 diseases [13]. In T2-weighted imaging, PSS often presents as solid lesions with heterogeneous signals [14]. In our study, the mixed STUMP group was younger and had a higher mean Ki-67 positive rate, while pure STUMP group cases had a higher rate of ER and PR expression.

Serum PSA, as a specific marker of prostate adenocarcinoma, is in the normal range or slightly elevated in STUMP patients. This might be because prostatic stromal tumors have no significant effect on prostatic epithelial cells (which produce PSA) or only cause a slight increase in PSA by tissue compression [13]. STUMP showed a mixed or high signal in T2-weighted imaging, while prostate adenocarcinoma showed a low signal in T2-weighted imaging [14]. In rare cases, STUMP may also be concurrent with prostate adenocarcinoma [13]. In addition, STUMP coexisting with PSS also needs to be differentiated from synovial sarcoma, rhabdomyosarcoma, and other sarcomas [15].

At present, there is no unified and clear treatment standard for STUMP. Because of the individual differences in the degree of STUMP, the treatment should be individualized, with close follow-up and good communication with patients. The age of the patient, size of the tumor, pattern of tumor growth, and degree of tumor invasion are important factors that affect the choice of treatment [16, 17].

RP provides hope for a radical cure in early-stage STUMP patients while avoiding the possibility of missed diagnosis of PSS by puncture. During surgery, the tumor should be removed as completely as possible. If the pa-

Table 5. Follow-up of STUMP patients

Patient No.	Age, years	Diagnostic specimen	Follow-up treatment	Follow-up time, months	State	Remarks
1	27	TURP	Re-TURP	78	Dysuria	No indwelling catheter
2	31	Needle biopsy	Surveillance	74	Stable	/
3	73	TURP	Lost[a]	/	/	/
4	67	Needle biopsy	TURP	68	Stable	/
5	66	RP	Lost	/	/	/
6	77	TURP	Lost	/	/	/
7	66	Needle biopsy	Prostatectomy	57	Stable	/
8	73	TURP	Surveillance	57	Stable	/
9	81	TURP	Surveillance	56	Stable	/
10	71	TURP	Re-TURP	56	Stable	/
11	71	Needle biopsy	Lost	/	/	/
12	51	RP	Surveillance	27	Stable	/
13	39	Needle biopsy	Surveillance	10	Stable	/
14	78	RP	Lost	/	/	/
15	58	Needle biopsy	Lost	/	/	/
16	53	RP	Surveillance	86	Stable	/
17	75	TURP	Surveillance	85	Stable	/
18	33	Needle biopsy	TURP	7	Dysuria	No indwelling catheter
19	37	RP	Surveillance and palliative treatment	16	Recurrence, dead	Combine with PSS
20	25	Needle biopsy	Prostatectomy	Lost	/	Combine with PSS
21	61	RP	Total pelvic exenteration	6	Recurrence	Combine with PSS
22	40	TURP	Radical cystectomy	24	Recurrence	Combine with PSS
23	23	TURP	Radical cystectomy	Lost	/	Combine with PSS

Patient Nos. 1–18 (N = 18): pure STUMP group; patient Nos. 19–23 (N = 5): mixed STUMP (STUMP coexisting with PSS) group. PSS, prostate stromal sarcoma; RP, radical prostatectomy; STUMP, stromal tumor with uncertain malignant potential; /, no data. [a] Lost: lost to follow-up.

tient is not eligible for radical surgery and has severe symptoms of urinary tract obstruction at the same time, TURP or cystostomy catheterization might be optional. Regular follow-up is required regardless of the treatment options. Watchful waiting could be an option for patients with limited slow-progress STUMP and who have no intention of surgery, but they should acknowledge the risk of disease progression and receive close follow-up. Relevant endocrine therapy could be considered according to the pathological results, but it is still controversial [18].

STUMP has a relatively good prognosis with occasional recurrence. Previous literature has reported that 2/3 of patients cannot be cured by an initial transurethral resection [2]. After treatment, patients had a 46% chance of local recurrence [19]. At the time of diagnosis, most lesions are confined to the prostatic lobe [7]. However, for patients with STUMP coexisting with PSS, the prognosis is relatively poor, along with higher risks of recurrence, metastasis, and disease progression [19]. In our study, the recurrence rate of STUMP increased significantly when STUMP coexisted with PSS.

To the best of our knowledge, this is the largest study to date on STUMP in a Chinese population. As a single-center retrospective study, our study has relevant limitations such as limited sample size and selection bias. Further multicenter, large-sample size, long-term follow-up studies are needed in the future.

Conclusion

STUMP is a rare disease with a relatively good prognosis. However, there is still a possibility of disease progression or coexistence with stromal sarcoma. Timely diagnosis and regular monitoring may be helpful in improving treatment outcomes.

Acknowledgements

We thank all the doctors at the Department of Urology at our hospital for allowing us to include their patients.

Statement of Ethics

This study was approved by the institutional Ethics Committee of our hospital. Patient records or information was anonymous and de-identified prior to analysis.

Conflict of Interest Statement

We declared that there was no conflict of interests.

Funding Sources

This study was supported by grants from the National Natural Science Foundation of China (Grant No. 81870518 to Wei Yu).

Author Contributions

Conception and design: S. Hu and J. Jin; administrative support: Y.S. Meng, X. Li, and Y.X. Xiao; provision of study materials or patients: W. Yu, Q. Shen, and Q. He; collection and assembly of data: Y. Fan, S.B. Li, and Y. Wang; data analysis and interpretation: Z.H. Zhou, Q. Zhang, and Z.Y. Lin; manuscript writing: Z.H. Liu, H.L. Song, S.M. Li, and Y.K. Chen; final approval of manuscript: all authors.

References

1 Yang W, Liu A, Wu J, Niu M. Prostatic stromal sarcoma: a case report and literature review. Medicine. 2018;97(18):e0495.
2 Gaudin PB, Rosai J, Epstein JI. Sarcomas and related proliferative lesions of specialized prostatic stroma: a clinicopathologic study of 22 cases. Am J Surg Pathol. 1998;22(2):148–62.
3 Mokhtari M, Homayoun M, Yazdan Panah S. The prevalence of prostatic stromal tumor of uncertain malignant potential in specimens diagnosed as prostatic hyperplasia. Arch Iran Med. 2016;19(7):488–90.
4 Sadimin ET, Epstein JI. Round cell pattern of prostatic stromal tumor of uncertain malignant potential: a subtle newly recognized variant. Hum Pathol. 2016;52:68–73.
5 Herawi M, Epstein JI. Specialized stromal tumors of the prostate: a clinicopathologic study of 50 cases. Am J Surg Pathol. 2006;30(6):694–704.
6 Moch H, Humphrey PA, Ulbright TM, Reuter VE. WHO Classification of Tumours of the Urinary System and Male Genital Organs. Geneva: WHO; 2016.
7 Murer LM, Talmon GA. Stromal tumor of uncertain malignant potential of the prostate. Arch Pathol Lab Med. 2014;138(11):1542–5.
8 Bidikov L, Maroni P, Kim S, Crawford ED. 67-year-old male with prostatic stromal tumor of uncertain malignant potential. Oncology. 2019;33(9):685007.
9 Hossain D, Meiers I, Qian J, MacLennan GT, Bostwick DG. Prostatic stromal hyperplasia with atypia: follow-up study of 18 cases. Arch Pathol Lab Med. 2008;132(11):1729–33.
10 Pan CC, Tsuzuki T, Morii E, Fushimi H, Chen PC, Epstein JI. Whole-exome sequencing demonstrates recurrent somatic copy number alterations and sporadic mutations in specialized stromal tumors of the prostate. Hum Pathol. 2018;76:9–16.
11 Latz S, Ellinger J, Goltz D, Marx C, Leuschner I, Müller SC, et al. Spindle cell rhabdomyosarcoma of the prostate. Int J Urol. 2013;20(9):935–7.
12 Vandoros GP, Manolidis T, Karamouzis MV, Gkermpesi M, Lambropoulou M, Papatsoris AG, et al. Leiomyosarcoma of the prostate: case report and review of 54 previously published cases. Sarcoma. 2008;2008:458709.
13 De Berardinis E, Busetto GM, Antonini G, Giovannone R, Di Placido M, Magliocca FM, et al. Incidental prostatic stromal tumor of uncertain malignant potential (STUMP): histopathological and immunohistochemical findings. Urologia. 2012;79(1):65–8.
14 Muglia VF, Saber G, Maggioni G, Monteiro AJ. MRI findings of prostate stromal tumour of uncertain malignant potential: a case report. Br J Radiol. 2011;84(1006):e194–6.
15 Konno M, Mitsuzuka K, Yamada S, Yamashita S, Kaiho Y, Ito A, et al. A case of adult metastatic rhabdomyosarcoma of the prostate cured by long-term chemotherapy with local radiation. Urol Int. 2019;102(1):118–21.
16 Michaud S, Moreau A, Braud G, Renaudin K, Branchereau J, Bouchot O, et al. [Prostatic Stromal Tumors of Uncertain Malignant Potential (STUMP): definition, pathology, prognosis and management]. Prog Urol. 2012;22(12):688–91.
17 Horie K, Takahashi Y, Ishida K, Tsuchiya K, Taniguchi M, Hagiwara N, et al. [Two cases of prostatic stromal tumor of uncertain malignant potential (STUMP) on pathological diagnosis after surgery for benign prostatic hyperplasia]. Hinyokika Kiyo. 2012;58(5):255–8.
18 Nagar M, Epstein JI. Epithelial proliferations in prostatic stromal tumors of uncertain malignant potential (STUMP). Am J Surg Pathol. 2011;35(6):898–903.
19 Klausner AP, Unger P, Fine EM. Recurrent prostatic stromal proliferation of uncertain malignant potential: a therapeutic challenge. J Urol. 2002;168(4 Pt 1):1493–4.