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Case study

Plasmacytoid acinar adenocarcinoma of the prostate: a newly described variant of prostate cancer

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Summary A plasmacytoid variant of prostatic adenocarcinoma has not been reported to the best of our knowledge. A 54-year-old male presented with recurrent attacks of acute urinary retention. Laboratory findings showed high creatinine and a serum prostate specific antigen of 50.7 μg/L. Magnetic Resonance Imaging showed a locally advanced tumor involving the bladder and extending to the base of prostate with bilateral ureterovesical junction involvement and invasion of the left seminal vesicle and left anterior mesorectal fascia as well as perirectal fat invasion. Diffuse metastases to the abdominopelvic lymph nodes were identified. Bone scintigraphy showed multiple bone metastases. Transrectal ultrasound guided biopsy of the prostate was attempted but the patient could not tolerate the procedure and the procedure was canceled. The patient then underwent transurethral resection of bladder tumor. Microscopic examination showed sheets of malignant cells with prominent plasmacytoid appearance undermining benign urothelium. The tumor cells were positive for PSA, PSAP, NKX 3.1 and Cytokeratin 8/18. The tumor cells were negative for P63, Cytokeratin 34βE12, Cytokeratin 20, Desmin, CD38, Kappa and Lambda light chains, Chromogranin, Synaptophysin, GATA 3, E-cadherin and CD45. INI1 was retained. Next generation sequencing showed an intermediate tumor mutational burden. Notably, no genomic alterations in the *CDH1* gene (encoding for E-cadherin) were present. The patient showed some initial response to antiandrogen therapy with a drop in serum PSA levels following androgen deprivation therapy. However, the patient died 6 months after diagnosis. It is critical to recognize this newly described variant and to distinguish it from plasmacytoid urothelial carcinoma. Recognition of the newly described plasmacytoid variant of adenocarcinoma of the prostate will lead to identification and reporting of more cases and a better understanding of its clinicopathologic features.

1. Introduction

Acinar adenocarcinoma of the prostate has many well recognized histological variants. Eight histological variants have been incorporated in the 2016 world health

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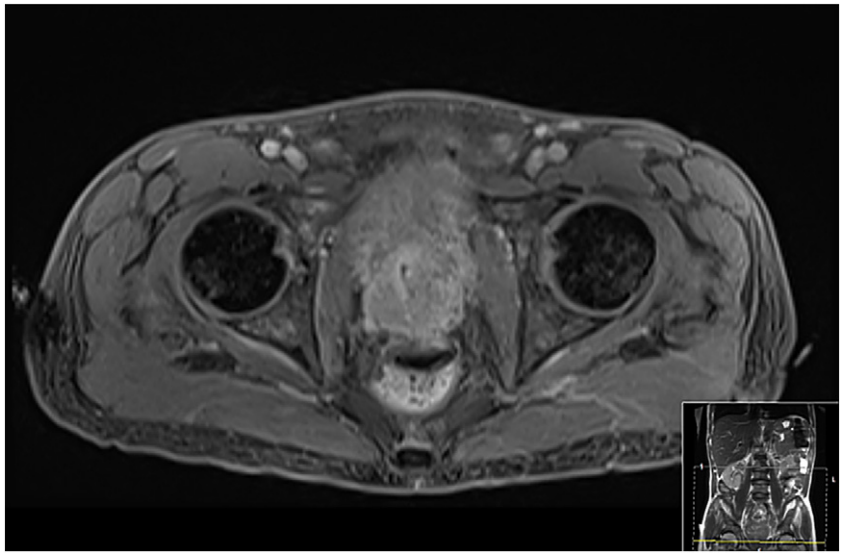

Fig. 1 Magnetic resonance imaging showed a locally advanced tumor involving the bladder and extending to the base of prostate.

organization (WHO) classification including atrophic, pseudo-hyperplastic, microcystic, foamy gland, signet ring–like cell, pleomorphic giant cell, and sarcomatoid [1]. Herein, we report a case of plasmacytoid variant of acinar adenocarcinoma of the prostate that has not been previously described.

2. Case report

2.1. Clinical history

A 54-year-old male with a history of hypertension was initially seen at a local hospital and found to have bilateral hydronephrosis. He was referred to one of the author's hospital with lower urinary tract symptoms including poor urine stream and dysuria along with recurrent acute urinary retention as well as bilateral severe flank pain and lower limb weakness. Following insertion of nephrostomy tubes, laboratory findings showed high creatinine (154 μmol/L) and high prostate specific antigen (PSA; 50.7 μg/L). Magnetic resonance imaging showed a locally advanced tumor involving the bladder and extending to the base of prostate with bilateral ureterovesical junction involvement and invasion of the left seminal vesicle and left anterior mesorectal fascia as well as perirectal fat invasion (Fig. 1). Diffuse metastases to the abdominopelvic lymph nodes were identified. Bone scintigraphy showed multiple bone metastasis (Fig. 2). Transrectal ultrasound guided biopsy of the prostate was attempted but the patient could not tolerate the procedure and the procedure was canceled. The patient then underwent transurethral resection of bladder tumor on July 2018. Following the diagnosis, the patient was started on bicalutamide followed by Lupron on the second week. The patient continued his follow up in a different hospital where he presented 1 month later with severe abdominal pain and underwent exploratory laparotomy and found to have large bowel obstruction with gangrenous caecum and right colon. A subtotal colectomy with end ileostomy was performed. His PSA was improving with treatment and the last PSA was 11.2 μg/L on December 2018. The patient died on January 2019, six months after diagnosis.

2.2. Pathologic findings

Gross examination showed multiple fragments of firm gray-tan tissue measuring in aggregate 1.5 × 1.2 × 0.3 cm. Virtually the entire specimen was involved by tumor. Microscopic examination showed sheets of malignant cells undermining benign urothelium. The cells had a prominent plasmacytoid appearance with eosinophilic cytoplasm and eccentrically placed hyperchromatic nuclei with small occasional nucleoli (Fig. 3A and B). Few mitotic figures were present. Immunohistochemical stains were performed on a Ventana Benchmark Ultra autostainer (Ventana Medical System, Tucson, AZ). The tumor cells were positive for PSA (Ventana; prediluted), PSAP (Ventana; prediluted), NKX 3.1 (concentrated; ACRIS Laboratories), and Cytokeratin 8/18 (Ventana; prediluted) (Fig. 3C-E). The tumor cells were negative for P63 (Ventana; prediluted), Cytokeratin 34βE12 (Ventana; prediluted), Cytokeratin 20 (Ventana; prediluted), Desmin (Ventana; prediluted), CD38 (Ventana; prediluted), Kappa and Lambda light chains (Ventana; prediluted), Chromogranin (Ventana; prediluted), Synaptophysin, GATA 3, E-cadherin (Fig. 3F), and CD45 (Ventana; prediluted). INI1 (BAF 47) (BD transduction Laboratories) was retained. The diagnosis was high grade prostatic adenocarcinoma Gleason score 5 + 5 = 10 (Grade Group 5) with prominent plasmacytoid features involving the bladder.

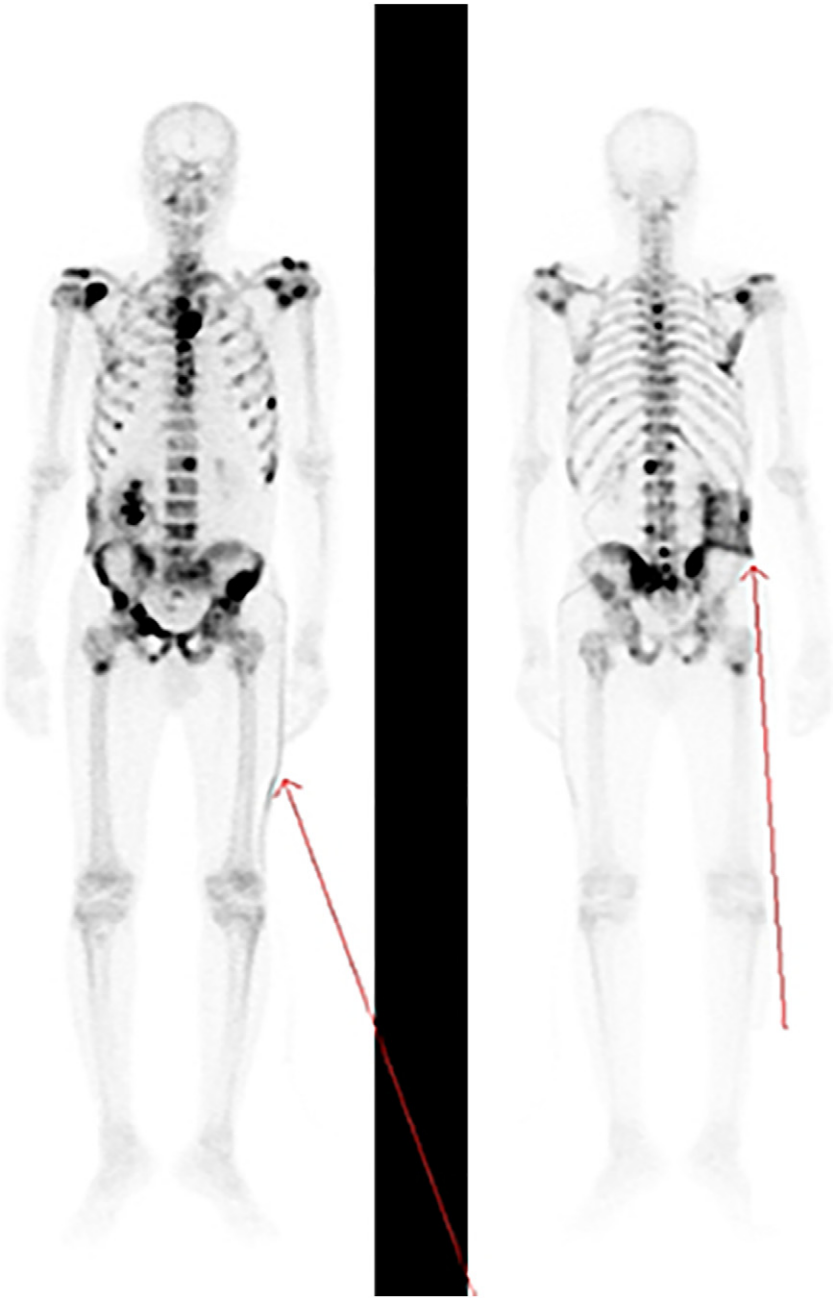

Fig. 2 Bone scintigraphy showed multiple bone metastasis.

2.3. Molecular findings

To determine genomic alterations present in this case, sequencing library covering the full coding regions of 644 cancer-associated genes were prepared and next generation sequencing was performed with a mean coverage of 726 reads on the HiSeq 2500 platform (Illumina, San Diego, CA) as described previously [2]. The tumor showed an intermediate tumor mutational burden with a tumor mutation rate of 7.91 mutations per megabase. Several putative driver alterations were identified, including missense mutations in *FANCA* (p.L1339F), *MET* (p.R547G), *SMARCA4* (p.Y820N), frameshifting deletions in *BRAF* and *KDR* and a large copy number loss involving the *RB1* locus (Table). Notably, no genomic alterations in the *CDH1* gene (encoding for E-cadherin) were present.

3. Discussion

Several variants of acinar adenocarcinoma of the prostate have been recognized. Pathologists should recognize these variants because some variants present diagnostic challenges while others have prognostic implications.

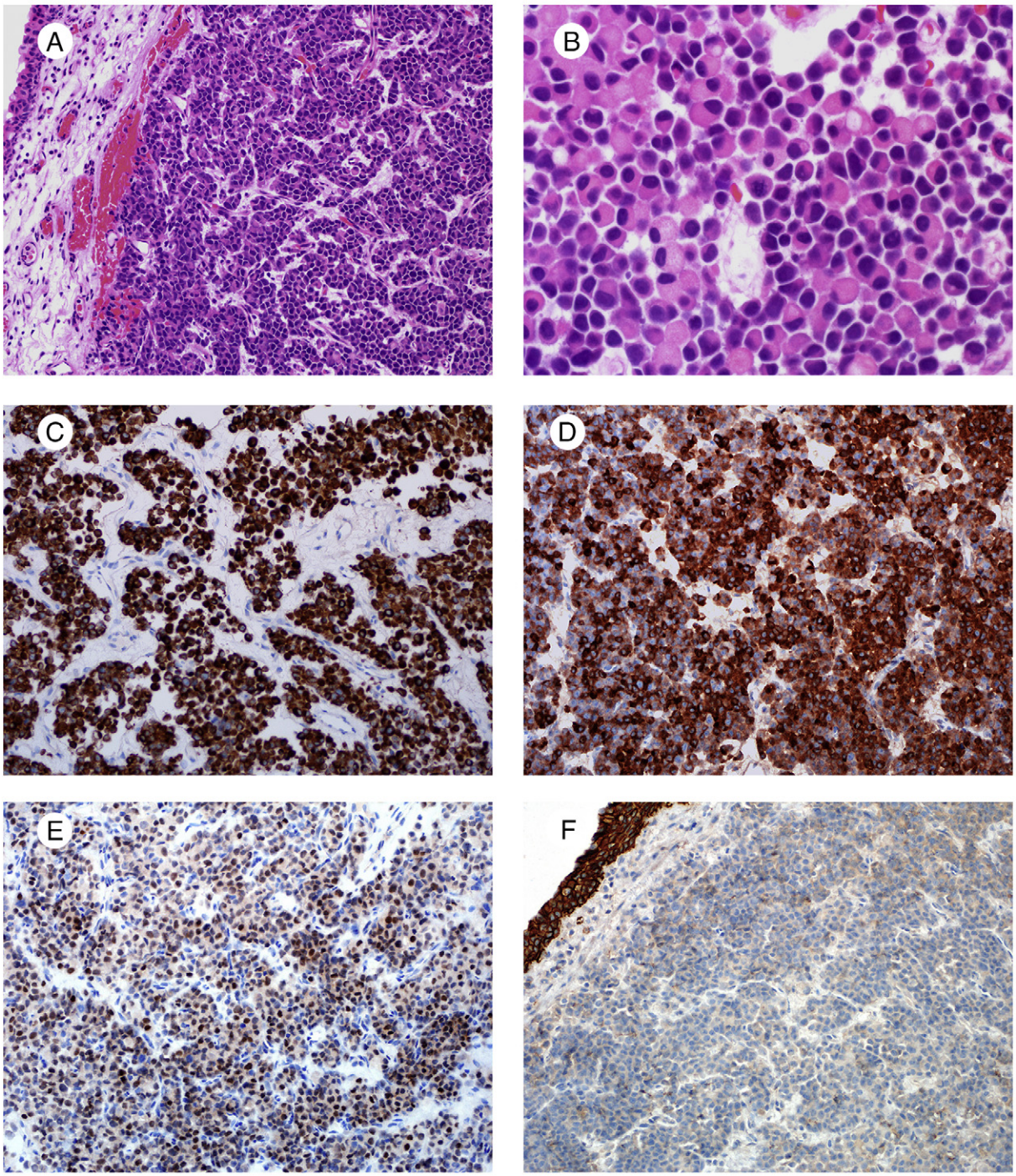

Fig. 3 A, Carcinoma undermining urothelium. B, Cells have a prominent plasmacytoid appearance. C, Tumor is diffusely positive for Cytokeratin 8/18. D, PSA immunohistochemistry was diffusely positive. E, NKX3.1 immunoreactivity was present in the majority of the tumor cells. F, Immunohistochemically, E-cadherin was lost in the tumor compared to intact staining in overlying urothelium.

Atrophic, pseudohyperplastic, microcystic, and foamy gland variants can mimic benign conditions and therefore pose diagnostic challenges [3-7]. Sarcomatoid variant of prostatic adenocarcinoma is an aggressive cancer [8,9]. Hansel et al reported 42 cases of sarcomatoid carcinoma of the prostate and approximately of half of patients developed metastatic disease and actuarial risk of death at 1 year after diagnosis was 20% [9]. Pleomorphic giant cell adenocarcinoma of the prostate is a highly aggressive variant with widespread metastasis and reported death soon after diagnosis [10,11]. Similarly, signet ring cell-like variant usually is an aggressive tumor with a mean survival

Table Next generation sequencing findings

Gene	Chr:Pos (hg19)	AA_change	%VAF
SNVs			
MET	chr7:116381017	p.R547G	56.21
ARID1B	chr6:157256668	p.E665D	48.44
CD58	chr1:117086957	p.M114 L	50.66
EP300	chr22:41545778	p.S798 N	51.66
FANCA	chr16:89805693	p.L1339F	46.23
FANCC	chr9:97873519	p.S480P	45.15
GPR124	chr8:37699181	p.V1109 M	36.11
IL7R	chr5:35876482	p.I425T	46.63
KDR	chr4:55961044	p.I966L	21.75
LRP1B	chr2:141739813	p.G935R	90.87
MAP3K6	chr1:27688031	p.L556 V	91.71
PCLO	chr7:82451900	p.K4901R	50.17
SETD2	chr3:47164223	p.I635V	47.78
SMARCA4	chr19:11129652	p.Y820N	43.03
SUZ12	chr17:30264357	p.V31E	44.04
SYNE1	chr6:152532698	p.R7507H	40.4
VHL	chr3:10183556	p.D9N	44.84
INDELs			
BRAF	chr7:140434409	p.G758Sfs*30	38
CUX1	chr7:101924116	p.S596_S598del	17.36
KDR	chr4:55961045	p.D958Hfs*3	19.73

Gene	Chromosome	Copy Number Variant
CNV		
RB1	chr13	−3.0844

Abbreviations: SNV, single nucleotide variant; CNV, copy number variant; AA, amino acid; VAF, variant allele frequency.

of 29 months [12]. Most cases of signet ring cell-like prostate cancers have the architectural pattern of Gleason patterns 4 and 5 which is in line with their adverse prognosis. Rarely, one can see signet ring cell-like vacuoles in well-formed glands of pattern 3, where the prognosis is favorable.

Plasmacytoid variant of prostatic adenocarcinoma has not been reported to the best of our knowledge. In contrast, plasmacytoid variant of urothelial carcinoma is a well-recognized entity. Plasmacytoid urothelial carcinoma is a rare aggressive high grade carcinoma with a lower median overall survival than comparable conventional urothelial carcinoma [13]. It is associated with high rate of recurrence and peritoneal involvement [14]. The current case demonstrated plasmacytoid features and initially was thought histologically to be plasmacytoid variant of urothelial carcinoma, given the lack of a morphological counterpart in the prostate. Not only was the morphology of the prostate tumor identical on H&E stains to the plasmacytoid variant of urothelial carcinoma, but the both plasmacytoid variants of the bladder and prostate share the distinctive feature of a loss of E-cadherin. The lack of E-cadherin typifies a group of invasive urothelial carcinomas that variably show plasmacytoid, rhabdoid, and signet ring cell features along with cells with a more central nucleus resembling lobular carcinoma of the breast. Only have an immunohistochemical work-up were we able to establish a definitive diagnosis of plasmacytoid variant of prostate adenocarcinoma. Of note, the *CDH1* locus, which encodes for E-cadherin did not show any genomic alterations, which suggests that other modes of gene inactivation are operative in this case. Indeed, several reports have demonstrated that *CDH1* undergoes frequent epigenetic silencing by promoter CpG island methylation in prostate cancer [15,16].

As in the bladder, our case was clearly associated with an aggressive clinical course, where the patient presented with locally advanced disease and multiple metastatic deposits and died after 6 months. That the patient showed some initial response to antiandrogen therapy with a drop in serum PSA levels following androgen deprivation therapy also supports the prostatic origin of this tumor.

Although the tumor was too advanced at presentation for the antiandrogen therapy to have any impact on survival, it is critical to recognize this newly described variant and to distinguish it from plasmacytoid urothelial carcinoma. Hopefully, in some cases the diagnosis of plasmacytoid variant of prostate adenocarcinoma can be established earlier in the course of the disease where therapy tailored to adenocarcinoma of the prostate may improve its prognosis. Recognition of the newly described plasmacytoid variant of adenocarcinoma of the prostate will lead to identification and reporting of more cases and a better understanding of its clinicopathologic features.

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