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Case report

Metastatic basal cell carcinoma of prostate in a young adult: A rare aggressive entity

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Abstract
Introduction: Prostate cancer is one of the commonest, malignancies affecting elderly males. Prostatic basal cell carcinoma, (PBCC) accounts for less than 0.01% of all prostate cancers.
Observation: A 32-year-old man presented with hematuria and lower urinary tract symptoms. Clinical examination showed hard, nodular enlarged prostate with multiple penile hard nodules. His prostate-specific antigen (PSA) level was 0.91 ng/mL. Histopathological examination of the fingerguided prostate biopsy revealed a malignancy with features of basal cell carcinoma. Further imaging studies were performed and metastases were found in both lungs, penis, pelvic lymph nodes and right ischium.
Conclusion: The current case highlights PBCC as a diagnostic pitfall which presented in a young adult with a normal PSA level.

Introduction

Prostate cancer is the second commonest malignancies affecting males worldwide [1]. It is usually considered as the disease of elderly but approximately 10% of the 241,740 men diagnosed with prostate cancer in 2012 represent early-onset prostate cancer defined herein as men diagnosed at 55 years of age or younger [2,3]. Adenocarcinoma is the most common histological subtype of prostatic carcinoma which arises from secretory cells of the glands [1]. The

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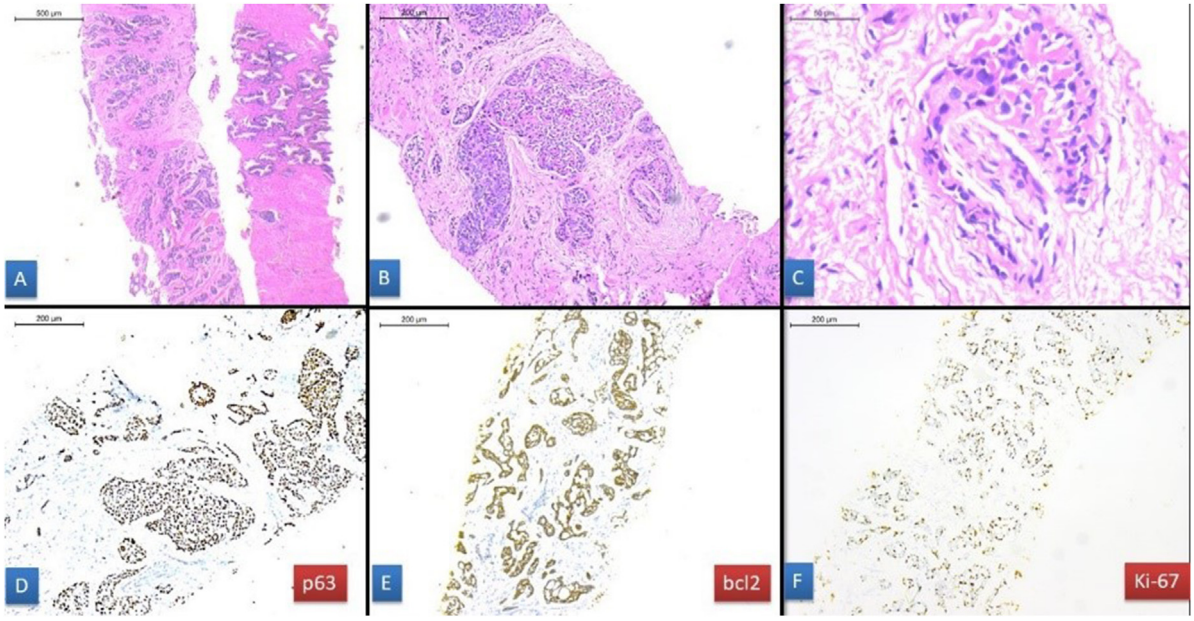

Figure 1 Panel of microphotographs of the prostatic core biopsy. (A) Histopathology of the prostatic core biopsies showing left core completely involved by the tumor cells (H and E, 4×); (B) Higher magnification shows basaloid cells arranged in nests with peripheral palisading (H and E, 10x); (C) The tumor cells show nuclear pleomorphism and perineural infiltration (H and E, 40×); (D, E, F) The tumor cells are p63 positive, bcl2 positive and Ki-67 index is around 80–85% (immunoperoxidase, 10×).

lesions arising from the basal cells of the gland are less common and can range from basal cell hyperplasia to a rare entity called as prostatic basal cell carcinoma (PBCC). PBCC cases comprise less than 0.01% of malignant prostate tumors [4–6]. Frankel and Craig [7] were the first one to describe this entity in the year 1974. This tumor has been variously named in the literature (adenoid cystic carcinoma, adenoid cystic-like tumor, basaloid tumor) but the current World Health Organization terminology is basal cell carcinoma [8]. Clinically, the patient usually presents with lower urinary tract symptoms and/or hematuria but can also presents with bladder outlet obstruction and metastasis [9]. Histopathology establishes the diagnosis but requires a careful distinction from its benign mimickers. The clinical behavior of PBCC remains unclear due to its rarity. Hence, no standard therapeutic approaches are currently established.

We present a case of 32-year-old man with PBCC with an insight into the histopathological and immunohistochemical (IHC) profile. The details of the clinical behavior and follow-up has been provided. The diagnosis of PBCC has many pitfalls, and hence, precise distinction from other mimickers is crucial for precise treatment.

Case report

A 32-year-old man presented to the Urology clinic with hematuria and lower urinary tract symptoms. Clinical examination revealed enlarged, hard, nodular prostate fixed to lateral pelvic walls and multiple hard nodules in the shaft of penis. The serum prostate-specific antigen (PSA) level was within normal limits (0.91 ng/mL). Ultrasound showed enlarged prostate (100 cc) with heterogeneous texture along with few ill-defined lesions measuring 5–9 mm. All other routine investigations were normal. The patient underwent finger guided prostate biopsy.

Microscopic examination of the biopsy specimen revealed a tumor arranged in nests, cords and cribriform pattern (Fig. 1A and 1B). Few foci of necrosis were also noted. The tumor cells show a moderate degree of anisonucleosis and pleomorphism. Perineural invasion was identified (Fig. 1C). A panel of immunohistochemistry markers was performed to identify the lesion as benign versus malignant and to confirm the basal cell phenotype. The tumor cells were strongly positive for p63 (nuclear) and bcl-2 (cytoplasmic) (Fig. 1D and 1E) and there was patchy positivity for 34βE12, thereby confirming their basal phenotype. These tumor cells were negative for CK20, PSA, CD117, and AMACR and hence ruling out acinar adenocarcinoma and other metastatic malignancies. Ki-67 proliferation rate was as high as 80–85% (Fig. 1F) indicative of malignant behavior. Thus, a diagnosis of PBCC was entertained.

T-weighted magnetic resonance imaging (MRI) revealed enlarged prostate with ill-marginated outline, extra-capsular extension, and infiltration into the base of bilateral seminal vesicles, the base of urinary bladder, anterior wall of rectum, anal canal and penis (Fig. 2, A & B). Gallium^{68} Prostate Specific Membrane Antigen (PSMA) PET-CT scan was also performed to look for the metastases. It revealed parenchymal and pleural nodules in bilateral lung fields, largest measuring 2 × 1.5 cm. Also, there were bilateral pelvic lymphadenopathy, solitary right ischium lesion and bilateral corpora cavernosum lesions on this PET-CT scan (Fig. 2, C, D & E).

Subsequently, the patient was started on Docetaxel chemotherapy with androgen deprivation therapy (injection leuprolide). Patient received four cycles of chemotherapy. However, in view of worsening clinical symptoms of penile pain with development of bilateral hydroureteronephrosis and deranged renal function, chemotherapy was stopped. Patient underwent bilateral percutaneous nephrostomy placement and received palliative radiation therapy to shaft of penis in view of persistent pain associated with metastatic priapism refrac-

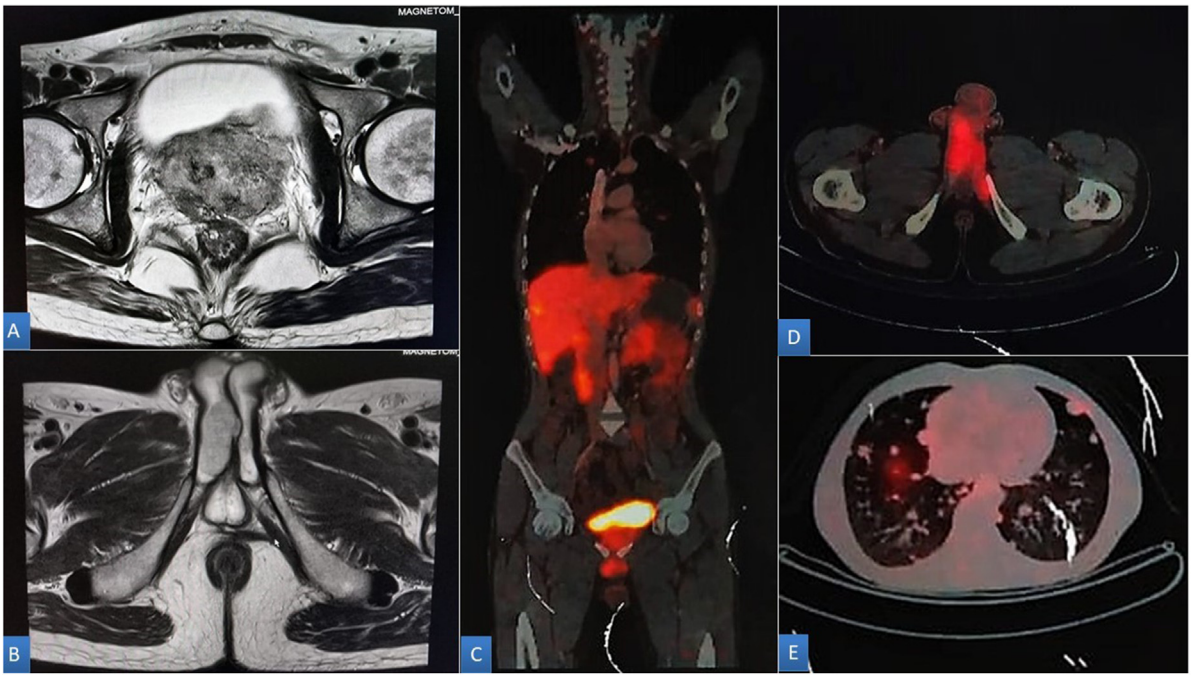

Figure 2 Panel of imaging studies highlighting the primary and metastatic lesions. T1 and T2 wted magnetic resonance images showing (A) altered signal intensity in the whole prostate with a poorly marginated hypointense focal lesion in left lobe and infiltration into bilateral seminal vesicles (left > right) and base of urinary bladder. Also, loss of fat plane with anterior wall of rectum is noted. (B) Hypointense ill-defined lesion involving bilateral corpora cavernosa with larger measuring 3.7 × 1.7 cm on right side. Gallium^{68} Prostate Specific Membrane Antigen (PSMA) PET-CT scan showing PSMA uptake in (C) prostate (SUV max 10.3), penis and lungs. (D) PSMA avid ill-defined lesions seen in bilateral corpora cavernosa, larger on the right. (E) PSMA avid parenchymal and pleural lesions in bilateral lung fields.

tory to analgesics. Further chemotherapy has been planned to be resumed once the palliative radiation therapy is completed.

Discussion

PBCC is a rare subtype of prostate carcinoma. Less than 100 cases have been reported since its description in 1974. The mean age at presentation is 50 years, ranging from 28 to 78 years [10]. PBCC is usually located in the transition zone [11].

Though PBCC is considered as a prostate carcinoma, PSA levels are usually normal, unlike adenocarcinoma because of its cell of origin being from basal layer [12]. This is one of the reasons that this entity has a low clinical suspicion of malignancy. Furthermore, in contrast to adenocarcinoma, the Gleason score is not used to grade the tumor due to the basal cell origin. The challenge for a histopathologist to diagnose this lesion is to differentiate it from benign mimickers like basal cell hyperplasia as well as sometimes from adenocarcinoma with a cribriform pattern. PBCC shows an infiltrative pattern, extra-prostatic extension, perineural invasion, necrosis, and stromal desmoplasia, unlike its benign mimickers. To identify the basal origin, immunostains like 34βE12 and p63 are helpful; to distinguish it from basal cell hyperplasia, bcl-2 and Ki-67 helps (high expression in PBCC) and to rule out adenocarcinoma, PSA immunohistochemistry is used. Also, metastatic urothelial carcinoma also needs to be ruled out with the help of CK20 [13]. Most of these differential diagnoses were ruled out in the current case based on these immunostains.

PBCC outcome is currently considered to be uncertain and depends upon the stage of the disease. Some tumors behave in a locally aggressive fashion, with the involvement of the bladder and periprostatic tissue and some others show metastatic disease to multiple organs [12]. Ali et al. [11], have suggested that basaloid pattern with large solid nests and necrosis is a feature of aggressive disease with adverse outcome.

Our case showed metastases to lungs, penis, pelvic lymph nodes along with bony metastasis indicative of poor outcome. Point of interest is that metastases often involve the liver, lung, and bowel but rarely reported in bone, as is commonly observed in prostate adenocarcinoma [14]. There are no consensus guidelines for the treatment of this malignancy owing to its rare occurrence. Various therapeutic modalities reported in the literature are radical prostatectomy, chemotherapy, androgen deprivation therapy, radiotherapy or combination of these [12]. The poor prognostic indicators are extra-prostatic extension/distant metastases [12]. A recent study investigated the molecular mechanism of this malignancy and showed it as an aggressive tumor with a frequent loss of phosphatase and tensin homolog (PTEN) expression and an over-expression of epidermal growth factor receptor (EGFR) [15].

Conclusion

Histopathology in conjunction with IHC is the gold standard for the definite diagnosis of prostatic basal cell carcinoma. Clinical suspicion of malignancy with a normal PSA level should alert a urologist to keep PBCC amongst one of the differential diagnoses of the rare

prostatic malignancies. Tumor necrosis, histologically pure PBCC, high Ki-67, and presence of metastasis remain important poor prognostic factors. However, the definitive therapy for this malignancy remains yet to be established.

Conflict of interests

None.

Authors' contributions (should include role and email address of each author)

GK: concept, collecting the data, collecting the literature, review of literature, writing the article; PR: concept, making of histopathological diagnosis, proof reading of manuscript; VSA: supervising the patient, collected the clinical images and critical analysis; UKM: supervising and treating the patient along with critical analysis.

Consent from the patient

Written consent was taken from the patient for treatment and surgical interventions including his counseling about the policies of the institute as an academic research and teaching hospital that allow publishing scientific data without identifying the patient identity or violating his confidentiality.

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