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Research Article

BIOPSY CONFIRMED BILATERAL TESTICULAR METASTASES IN A PATIENT WITH STAGE 4 PROSTATE CANCER, DESPITE NEGATIVE FINDINGS REPORTED ON STANDARD PSMA PET/CT IMAGING.

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Abstract: ***Introduction:*** Metastatic disease to the testicles from solid tumors is exceedingly rare, with retrospective autopsy studies reporting a prevalence of only 0.68% of patients. Metastatic carcinomas to the testicles typically present as solitary and unilateral lesions, which may mimic primary neoplasms in appearance, emphasizing the need for careful diagnostic evaluation. The 60-year-old male patient initially presented with symptoms of incomplete voiding and nocturia for six months. Further examination revealed grade 2 prostatomegaly with asymmetrical hard consistency and nodularity on digital rectal examination and raised PSA levels, alongside hard consistency and thickened palpable spermatic cord structures on bilateral testes examination. MP MRI Prostate and TRUS biopsy confirmed prostate acinar adenocarcinoma. Ultrasound of the testes suggested possible testicular malignancy. 68 Ga PSMA PET CT confirmed prostatic lesions with metastases in both seminal vesicles and enlarged pelvic, abdominal, mediastinal, and left supraclavicular regions with negative avidity in bilateral testicles. The patient underwent channel laser TURP and bilateral high inguinal orchidectomy. Histopathology examination indicated deposits of adenocarcinoma of primary prostate origin in bilateral testes, epididymis, and rete testis, with involvement of the bilateral tunica albuginea. Prostatic chips confirmed acinar adenocarcinoma, conventional, with a Grade Group of 5 (Gleason score 4 + 5 = 9). This case report highlights the limitation of 68Ga-PSMA PET/CT in detecting unusual metastatic lesions to bilateral testicles from Prostate Cancer.

Keywords: PSMA: prostate specific membrane antigen, PET: positron emission tomography, CT: computed tomography MP MRI: multiparametric magnetic resonance imaging, USG: ultrasonography

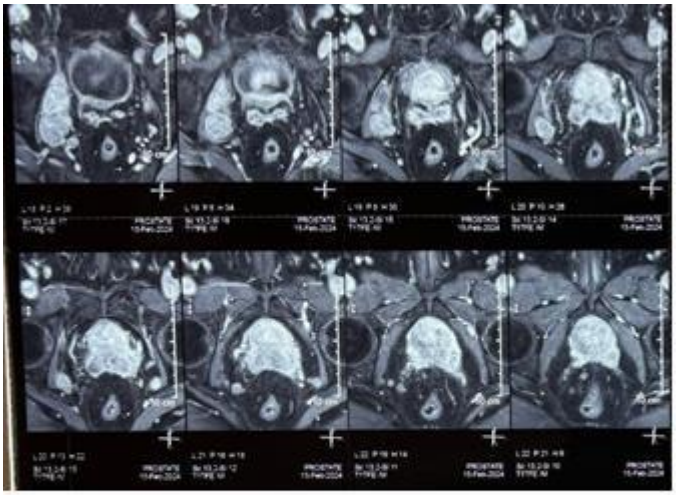
INTRODUCTION

Prostate cancer stands as a significant contributor to morbidity and mortality in the Western world, ranking as the second most common cancer among men globally. Its metastasis typically targets the pelvic and retroperitoneal lymph nodes, the skeletal system, lungs, and liver, delineated by M1A (non-regional lymph node metastases), M1B (bone metastases), and MIC (visceral metastases) sub-stages1. Notably, the presence of visceral metastases indicates aggressive tumor biology with an unfavourable prognosis 2,3

CASE PRESENTATION

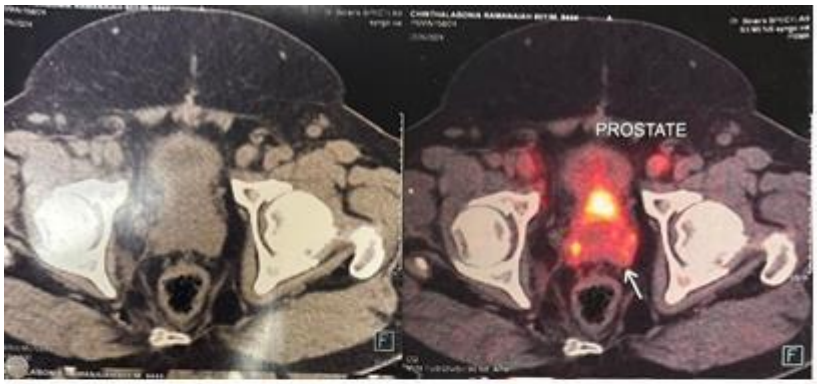
Study Design and Reporting Standards

The 60-year-old male patient initially presented with symptoms of incomplete voiding and nocturia for six months. Further examination revealed grade 2 prostatomegaly with asymmetrical hard consistency and nodularity on digital rectal examination, alongside hard consistency and thickened palpable spermatic cord structures on bilateral testes examination. Initial evaluation, including USG KUB and biochemical investigations, indicated cystitis, significant PVR, and elevated PSA levels. MP MRI prostate revealed a nodular heterogeneous lesion in the left peripheral zone involving the left seminal vesicle. Ultrasound of the testes suggested possible testicular metastasis. Tumor markers were unremarkable.

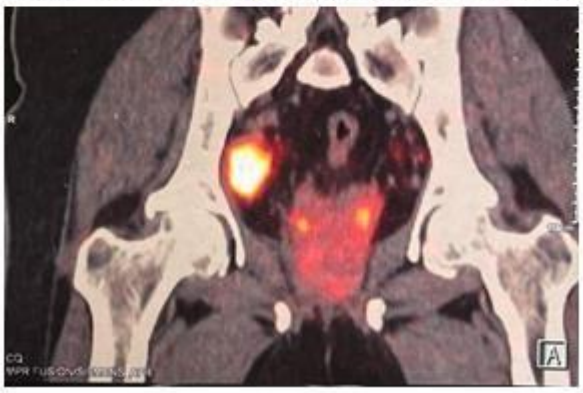


MP MRI PROSTATE SHOWS LEFT PERIPHERAL ZONE PIRADS V LESION AT THE BASE OF PROSTATE WITH INVOLVEMENT OF LEFT SEMINAL VESICLE. EPE PRESENT.

Subsequent 68 Ga PSMA PET CT confirmed prostatic lesions with metastases in both seminal vesicles and enlarged pelvic, abdominal, mediastinal, and left supraclavicular regions.



`WHOLE BODY CT SCAN WAS PERFORMED INITIALLY. 2.5 mCs gA 68 psma WAS ADMINISTERED IV AND WHOLE BODY IMAGES WERE ACQUIRED AT 60 MINUTES USING DISCOVERY 610 SYSTEM.



Following the metastatic findings, TRUS biopsy revealed prostatic acinar adenocarcinoma affecting both lobes, with a Gleason score of 3+5=8, Grade Group V. The patient underwent channel laser TURP and surgical resection of metastases via bilateral high inguinal orchidectomy. Histopathology examination indicated deposits of adenocarcinoma of primary

prostate origin in bilateral testes, epididymis, and rete testis, with involvement of the bilateral tunica albuginea. Lymph vascular invasion and perineural invasion were also observed. Prostatic chips confirmed acinar adenocarcinoma, conventional, with a Grade Group of 5 (Gleason score 4 + 5 = 9).

DISCUSSION

Prostate cancer stands as a significant contributor to morbidity and mortality in the Western world, ranking as the second most common cancer among men globally. Its metastasis typically targets the pelvic and retroperitoneal lymph nodes, the skeletal system, lungs, and liver, delineated by M1A (non-regional lymph node metastases), M1B (bone metastases), and M1C (visceral metastases) sub-stages1. Notably, the presence of visceral metastases indicates aggressive tumor biology with an unfavorable prognosis 2,3

For over three decades, diagnostic investigations have relied on physical examinations, including the digital rectal examination (DRE), blood tests measuring PSA levels, and various biopsy methods, whether trans-rectal, trans- perineal, blind, or image-directed. Imaging techniques, predominantly CT scans, and more recently, multiparametric MRI and PET/CT scans, have augmented the diagnostic arsenal, providing additional insights into disease progression and management 4,5

Prostate cancer cells exhibit heightened expression of a surface marker called Prostate Specific Membrane Antigen (PSMA). Initially, antibodies were developed, followed by peptides, to target this antigen, forming the basis for prostate cancer-specific molecular imaging agents 6

PSMA, a 750-amino acid transmembrane protein, typically resides within the apical epithelium of secretory ducts in benign prostatic tissue. Its physiological role remains uncertain, while its enzymatic function involves cleaving -linked glutamate from N-acetyl aspartyl glutamate and -linked glutamates from polyglutamate folates. During malignant transformation, PSMA relocates to the luminal surface of the ducts, resulting in overexpression. This overexpression is not observed in benign conditions like prostatic hyperplasia 6

Despite its presence in other tissues, PSMA has emerged as an excellent agent for targeted imaging and therapy, given its robust overexpression in 95% of prostate cancer cells. While it is not prostate-specific, PSMA is also expressed in various other tumors and tissues. PSMA expression correlates with advanced disease, castrate-resistant disease, Gleason score, and PSA level 7,8

Small molecule PSMA-peptide inhibitors, also known as ligands, have been developed, showing high binding affinity and forming the cornerstone of current PSMA imaging techniques. Three peptide ligands have become predominant in clinical use, with one labelled exclusively with 68Ga and two labeled with either 68Ga or 177Lu, offering a theranostic approach to prostate cancer when desired 9,10,11

The development of these agents has been guided by a rational approach, focusing on key parameters such as PSMA affinity (and thus tumor uptake) and rapid blood clearance. GLU-NH-CO-LYS-(AHX) [68GA-HBED-CC) (HBED CC: N.NO-BIS(2-HYDROXY-5-(ETHYLENE-BETACARBOXY) BENZYL)

ETHYLENEDIAMINE N,NO-DIACETIC ACID), also known as 68GA-

PSMA-11, is widely used for prostate cancer PET/CT imaging. The HBED chelator forms a stable complex with Ga, resulting in fast blood clearance, low liver uptake, and high uptake in PSMA-expressing tissues 12,13,14

Recent investigations have explored the potential of 68GA-PSMA PET/CT as a staging modality in primary prostate cancer. Since cellular PSMA expression correlates with PSA and Gleason score, and 68GA-PSMA PET/CT has shown superiority over standard staging modalities like CT, its use in staging primary disease appears logical. Early data support this notion, with several studies demonstrating high rates of detection of CT occult early metastatic disease 15

CONCLUSION

It's noteworthy that metastatic disease to the testicles from solid tumors is exceedingly rare, with retrospective autopsy studies reporting a prevalence of only 0.68% of patients. Metastatic carcinomas to the testicles typically present as solitary and unilateral lesions, which may mimic primary neoplasms in appearance, emphasizing the need for careful diagnostic evaluation.[16,17]. Ga 68 PSMA PET CT serves as limitation in diagnostic evaluation of suspected testicular metastases.

DATA AVAILABILITY

All data underlying the result are available as part of the article and no additional source data are required.

CONSENT

Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient/parent/guardian/relative of the patient.

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