Case study

Unusual presentations of Metastases in Carcinoma prostate

1. ABSTRACT

Aim: The prognosis in prostate cancer mainly depends on presence or absence of metastases. Two patients presented to us with non specific signs and symptoms. Detailed history and examination could not help us to make any diagnosis. The histopathological examination of the biopsies at different sites led us to the diagnosis of prostate carcinoma. Our objective is to learn and introduce the rare presentations of metastases in carcinoma prostate

Case presentation: We present two unusual presentations of metastases in carcinoma prostate which were not suspected during the initial routine evaluation. One was a 75 yr male who presented with penile nodules which was later diagnosed to be carcinoma prostate. Other was a 76 year old man who had upper limb neuropathy which led us to the diagnosis of carcinoma prostate. The modes of presentation of these cases completely misled our evaluation and management protocol.

Discussion: Metastasis to penis occurs commonly from primaries in genitourinary tract: bladder (28.6%) and prostate (27.9%) followed by gastrointestinal tract. Metastatic spinal cord tumors occur in 10% of all cancer patients. Cervical spine involvement is relatively uncommon, accounting for less than 10% of all spinal metastases. The most prevalent primaries which metastasize to spinal cord are lung, breast, prostate, kidney, and thyroid.

Conclusion: Overall survival in prostate carcinoma depends on early detection and management. Despite these rare presentations of prostatic carcinoma, urologists should have

high index of suspicion coupled with low threshold for investigations so that early diagnosis and management is possible.

2. KEYWORDS:

Case report, Prostate cancer, Penile nodule, Skeletal metastases, Cervical Spine, Immunohistochemistry, Chemohormonal therapy.

3. LIST OF ABBREVIATIONS

BCG - Bacillus Calmette Guerin

TURP - Transurethral resection of prostate

Cms - Centimeters

DRE - Digital rectal examination

TRUS - Transrectal ultrasound

NAF - Sodium fluoride

GnRH - Gonadotropin releasing hormone

HPE - Histopathological examination

IHC - Immunohistochemistry

TWOC - Trial without catheter

PSMA - Prostate specific membrane antigen

4. INTRODUCTION:

Prostate cancer is a growing concern in global epidemiology. More than one million cases are diagnosed annually, and the mortality burden has risen to over three lakh deaths per year.

Prostate cancer has become the fifth leading cause of cancer death among men. Commonly, low risk disease is often discovered through routine prostate cancer screening or when patients present with lower urinary tract symptoms. However some patients can present with advanced metastatic disease with limited and non-specific symptoms. These are the ones who need detailed evaluation in order to find out the cause and treat it appropriately. Overall survival in prostate carcinoma depends on early detection and management. We came across with two such patients in whom the modes of presentation completely misled our evaluation and management protocol.

5. CASE PRESENTATION:

Case I: A Seventy five year old male presented to our outpatient department with complaints of a growth on the glans penis and poor flow since two months with mild voiding symptoms. He was diagnosed to have Urothelial carcinoma of bladder in 1997 for which he had received intravesical Bacille Calmette Guerin (BCG) therapy. He also had undergone Transurethral resection of prostate (TUR-P) in 1999 the histopathology of which was benign. Examination revealed a five centimeters (cms) cauliflower like growth in the glans penis close to meatus with palpable nodules in the proximal four centimeters of urethra (figure 1). External urethral meatus was narrow. Digital rectal examination (DRE) revealed a normal firm prostate. Systemic examination was normal. With a clinical suspicion of penile carcinoma, a wedge biopsy was performed which turned out to be adenocarcinoma. Primary adenocarcinoma of penis is exceedingly rare and so we suspected that these nodules could be metastatic deposits from a different primary. During evaluation to check for the primary site of carcinoma, serum PSA was reported as more than 100 ng/ml. He underwent standard twelve core Trans rectal

Ultrasound (TRUS) guided prostate biopsy. The biopsy reported adenocarcinoma prostate with Gleason 4+5 with all twelve cores positive for the carcinoma. On further evaluation 18F-Sodium Fluoride (NAF) bone scan did not show any bony metastases. He was advised chemohormonal therapy due to presence of visceral metastases and was started on Gonadotropin releasing hormone (GnRH) agonist, Leuprolide 45 mg with six cycles of docetaxel chemotherapy. The penile growth and nodules gradually started showing regression after six cycles (figure 2) with significant improvement in voiding.

Figure 1: Penile growth and nodules before treatment

Figure 2: Penile growth and nodules after treatment

Case II: A Seventy six year old male developed numbness in his right index finger with tingling and pricking sensations for one month. He was evaluated by a Neurologist as the numbness was persistent and not responding to conservative treatment. MRI of the cervical spine was done which showed an Intradural extramedullary spinal mass at C_5-C_6 and C_6-C_7 vertebral level (figure 3). Cervical laminectomy with excision biopsy of the mass was performed. HPE of the mass revealed adenocarcinoma with Immunohistochemistry (IHC) staining positive for PSA. IHC staining of other markers were all negative. He developed

acute retention of urine after the procedure and failed trial void without catheter (TWOC). DRE revealed a hard prostate and serum PSA was 428 ng/ml. Gallium 68 Prostate specific membrane antigen (Ga^{68}-PSMA) PET CT revealed multiple skeletal and lymph nodal metastatis. He also had a vesical calculus for which he underwent Channel TUR-P with cystolithotripsy. He was started on GnRH agonist (Leuprolide 45 mg) with six cycles of docetaxel chemotherapy. He is stable on follow up and PSA after 3 months was 1.3 ng/ml.

Figure 3: T2-MRI cervical spine showing mass at C5-C7 level causing compression of spinal canal (arrows)

6. DISCUSSION:

Prostate cancer is the second most frequently diagnosed cancer of men after lung cancer and the fifth most common cancer worldwide. The axial skeleton, the nodes of the pelvis and the retroperitoneum are the most frequent sites of metastasis. Bony and regional lymph nodal metastases comprise of 66.8% and 68%, respectively, in autopsied cases.[1] Other rare sites of

metastases from prostate cancer include lungs (49.1%), bladder (39.2%), liver (35.6%) and adrenals (17.3%).[2] The incidence of cervical lymph node involvement is very rare and has been reported as 0.4% or less. Hematogenous, lymphatic, and direct infiltrations are the typical routes of spread. Metastasis to penis occurs commonly from the primaries in genitourinary tract: bladder (28.6%) and prostate (27.9%) followed by gastrointestinal tract. Metastatic spread from the prostate to the penis occurs by many routes like retrograde venous or lymphatic spread, and direct extension.[3] The most reliable diagnostic modality remains either needle or excision biopsy which allows for histological and immunological confirmation of metastatic spread, and evaluation of extent of invasion.[4] Most of these metastatic deposits present as persistent penile pain or priapism with voiding symptoms. Only about 7 % present in the form of penile nodules thereby mimicking a primary penile cancer.[5] The treatment varies from surgical excision to chemotherapy and radiotherapy.

Metastatic spinal cord tumors occur in 5 to 10% of all cancer patients. Cervical spine involvement is relatively uncommon, accounting for less than 10% of all spinal metastases. The most prevalent primaries which metastasize to spinal cord are lung, breast, prostate, kidney, and thyroid. Most patients presenting with cervical spinal cord tumors generally present with upper limb numbness and weakness. Radiation therapy, surgery, or combination, are the primary treatment modalities. Emphasis should be on palliative treatment and improving quality of life in view of the poor prognosis in such cases.

7. CONCLUSION:

There are anecdotal reports about rare presentations of carcinoma prostate like involvement of supraclavicular lymph nodes, ureteric adventitia etc. Although these are rare cases, the overall survival depends on early detection and treatment with androgen deprivation therapy

and chemotherapy. PSA immunohistochemical staining is very useful in doubtful histopathological examination of metastatic deposits. DRE which is an essential part of examination in elderly man is often forgotten. It should be done regardless of the presenting symptoms and the provisional diagnosis. Screening for prostate cancer by measuring PSA will help in early diagnosis. Despite these rare presentations of prostatic carcinoma, urologists should have high index of suspicion coupled with low threshold for investigations so that early diagnosis and management are done.

8. **INFORMED CONSENT**: All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent will be made available for review by the Editorial office/Chief Editor/Editorial Board members of this journal if needed.
9. **ETHICAL APPROVAL**: All authors hereby declare that all experiments have been examined and approved by the NU Hospitals ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.
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