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. 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 hundred thousand 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.

4. 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 known diabetic for past 15 years on regular medications and follow up. His sugars

were well controlled. 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 also complained of significant loss of appetite and weight for past 3 months. He did not have any comorbidities but was very obese. 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)

5. 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]. Lymph nodes which are commonly involved in metastatic prostate cancer are hypogastric and obturator

lymph nodes. Further spread rarely can occur through rich lymphatic network of retroperitoneal and para-aortic nodes, then to Cisterna chyli, to the thoracic duct, and then to the left subclavian vein into systemic circulation. This has lymphatic extension from left supraclavicular nodes which can result in metastases.[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.

Prostate carcinoma can also present in various unusual and atypical forms like huge abdominal lump, malignant ascites and peritoneal metastasis.[3,4] Salako et al[5], in his original article published in 2019 reported thirteen patients who had unusual presentations of prostate carcinoma. Five had left supraclavicular swellings, while four had haematochezia and tenesmus. Others included large bowel obstruction requiring emergency colostomy and a scalp mass. Other rare sites of metastases from prostate cancer include lungs (49.1%), bladder (39.2%), liver (35.6%) and adrenals (17.3%).[6]

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.[7] Theoretically, prostatic adenocarcinoma may be confused with penile glandular tumors of penis. But the latter tumors originate from the paraurethral Littre glands and present with conspicuous mucinous features. These features are not typically seen in prostatic tumors.[8] 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.[9]

Magnetic resonance imaging yields higher accuracy in the differential diagnosis of penile metastases in comparison to ultrasonography or Computed Tomograph.[10] Fine needle aspiration cytology (FNAC) can also be useful as an initial diagnostic approach. The detection of "cercariform cells" in a FNAC sample of a penile tumor strongly suggests an urothelial origin.[11] 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.[12] There are a number of treatment options depending on the general status of the patient, location and extent of the primary tumour and symptomatology. These include local excision, radiation therapy, bilateral orchiectomy, hormonal manipulation, systemic chemotherapy and partial/total amputation of the penis in severely symptomatic cases like intractable pain, uncontrollable bleeding etc.[13]

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. Osseous metastases occur in 90% of metastatic prostate cancer cases, with the spine being the most common site. The predilection of prostate cancer for metastases to the spine is commonly owing to the spread via Batson plexus of valveless veins located in the epidural space between vertebral column and dura matter.[14] In an autopsy study by Bubendorf et al[15] in 2000, one-third of prostate cancer cases were found to have hematogenous spread. This study reiterated the classical hematogenous spread via the vena cava, but also identified upward metastatic spread along the spinal veins after metastasization to the lumbar spine, which was hypothesized to occur early in the metastatic process.

Nearly one third of prostate cancer spinal metastases are symptomatic and manifest with either intractable pain, neurological deficits from nerve root or spinal cord compression and mechanical instability, which sometimes require surgical intervention.[16] Conventionally, fractionated external beam radiation therapy is widely utilized in the palliative treatment of spinal metastases from prostate cancer.[17] There are many retrospective studies in literature which show that stereotactic body radiation therapy has gradually emerged as a promising treatment strategy for spinal metastases from prostate cancer.[18]. Radiation therapy becomes very important to promote local control where there is concern for impending cord compression or intractable bony pain.[19]

Although these are rare cases, the overall survival depends on early detection and treatment with androgen deprivation therapy and chemotherapy. Serum PSA and DRE are the two most important methods for screening and diagnosis of prostatic carcinoma in unusual situations like this.[20]. IHC will further help in confirmation. Emphasis here should be on palliative treatment and improving quality of life in view of the poor prognosis in such cases.

6. CONCLUSION:

There are anecdotal reports about rare presentations of carcinoma prostate like involvement of supraclavicular lymph nodes, ureteric adventitia etc. PSA immunohistochemical staining is very useful in doubtful histopathological examination of metastatic deposits from unknown primary. DRE which is an essential part of examination in elderly man is often forgotten and ignored. It should be done regardless of the presenting symptoms and the provisional diagnosis. Screening for prostate cancer by measuring PSA in patients presenting with LUTS 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.

7. **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.
8. **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.
9. **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

FNAC - Fine needle aspiration cytology

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