

Case Report

Splenic Metastases in Prostate Adenocarcinoma - A Case Report with Radiological Review of Patterns of Metastases in Prostate Adenocarcinoma

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ABSTRACT

A Ca prostate account for about 25% of new cancers in men. Ca prostate metastases occurs by direct spread, lymphatic spread and haematogenous spread. Direct spread occurs to adjoining organs. Lymphatic spread occurs to lymph nodes. Haematogenous spread commonly occurs in bones and rarely in lungs, liver, brain, spleen, adrenal glands, kidneys, muscles, pancreas, and salivary glands. Liver, spleen and lungs are atypical metastatic sites of CA prostate. We present a case of 58 years old male patient presenting with multiple retroperitoneal lymph nodes, extensive mixed osteoblastic and osteolytic skeletal metastases and multiple splenic metastases.

Keywords: Ca prostate, osteoblastic, splenic metastases, retroperitoneal lymphadenopathy.

INTRODUCTION

Prostate cancer is the second most common cancer in men after lung cancer and fifth most common cancer worldwide. ^[1] Ca prostate accounts for about 25% of new cancers in men. ^[2] Ca prostate metastases occur by direct spread, lymphatic spread and haematogenous spread. Direct spread occurs to adjoining organs - urinary bladder, seminal vesicles, urethra and rectum. Lymphatic spread occurs to lymph nodes. Haematogenous spread commonly occurs in bones. Rarely does it occur in lungs, liver, brain, spleen, adrenal glands, kidneys, muscles, pancreas, and salivary glands. ^[3] 85% of patients with metastatic prostatic carcinoma show skeletal involvement. Atypical metastases site (defined as metastases localising to sites other than bones or lymph nodes outside pelvis and abdomen) is 10.6% in distinct lymph nodes, 10.2% in liver and 9.1% in thorax. ^[4]

CASE REPORT

A 58 year old male patient presented with difficulty in micturition since 1 month, feeling of incomplete micturition with hesitancy and increased frequency. No H/o burning micturition or hematuria. He also gave history of low back ache since 3 months.

Urine showed: 20-30 RBCs/hpf and 6-8 pus cells/hpf, Blood urea level: 71 mg/dl, Blood urea nitrogen: 33, Serum creatinine: 1.49 mg/dl, Serum PSA: 2671.05 ng/ml. Thus, blood urea nitrogen and PSA were raised.

ON USG, prostate was enlarged, measuring approx. 4.0 (L) x 3.8 (AP) x 4.5 (T) cms (Prostatic weight: 35.5 gms.) and showed heterogeneous echotexture with multiple small anechoic areas of necrosis (Figure 1a and b). Prostatic outlines were smooth and intact. Both seminal vesicles appeared normal. There was suspicion of

invasion of urinary bladder base. Multiple discrete retroperitoneal lymph nodes of heterogeneous echotexture of sizes 1-3 cm were noted in left para-aortic, inter aorto-caval, retro-caval and pre-caval region (Figure 2). Most of them showed central small anechoic areas of necrosis. Largest lymph node was noted in pre-caval region

measuring approx. 3.2 x 2.2 x 4.8 cms. Multiple right internal iliac lymph nodes of size 1-1.5 cms were also noted. Mild splenomegaly was noted (Craniocaudal extent 14.5 cm) and showed multiple well defined hypoechoic solid lesions of various sizes (0.3 cm - 1.5 cm) - suggestive of splenic metastases (Figure 3a and b).



Figure 1a

Figure 1b

USG prostate transverse (1a) & longitudinal section (1b) showing enlarged prostate with heterogeneous echotexture with invasion of urinary bladder base.

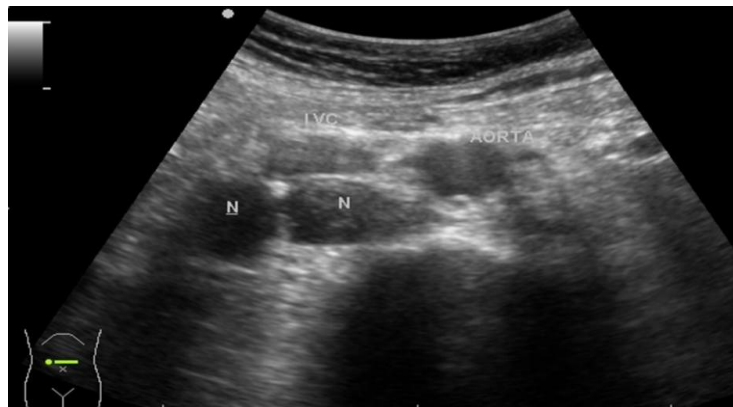


Figure 2: USG abdomen (retroperitoneal region) showing multiple discrete retroperitoneal lymph nodes in paracaval and retrocaval region.



Figure 3a

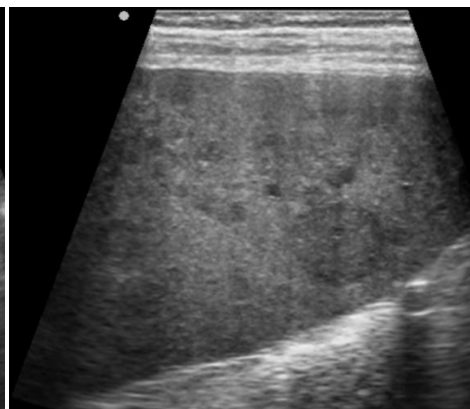


Figure 3b

USG spleen (1a: 3.5, 1b:8 MHz probe) showing multiple hypo echoic lesions scattered in entire spleen suggestive of metastases.

CT ABDOMEN AND PELVIS: showed prostatic enlargement [4 (CC) x 3.9 (AP) x 4.9(T) cms.], showing heterogeneous density with heterogeneous enhancement with contrast, intact prostatic outlines and peri-prostatic fat planes with elevation of bladder base (Figure 4). Multiple variable size enhancing discrete lymph nodes were noted in left para-aortic, inter-aortocaval, retro-caval and pre-caval region (Figure 5a

and b). Spleen was enlarged with multiple variable sized non-enhancing hypodense lesions - suggestive of metastases (Figure 6a and b). Visualised lower ribs, sternum, lower scapulae, dorsal and lumbar vertebral bodies, pelvic bones, sacrum, bilateral femoral head and neck showed mixed osteoblastic and osteolytic lesions - suggestive of metastases (Figure 7a and b).



Figure 4a

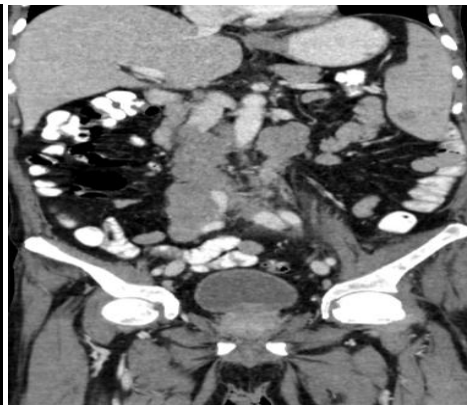


Figure 4b

Sagittal (4a) and coronal (4b) contrast enhanced abdomen & pelvis showing enlarged prostate with heterogeneous density elevating urinary bladder base, multiple retroperitoneal left para-aortic and right para-caval nodes and multiple splenic metastases.



Figure 5a



Figure 5b

Axial CECT abdomen (5a & 5b) showing multiple discrete heterogeneously enhancing metastatic retroperitoneal lymph nodes in left para-aortic, retro-aortic, right para-caval region.



Figure 6a



Figure 6b

Axial (6a) and coronal (6b) CECT abdomen showing multiple hypodense lesions in entire spleen - suggestive of metastases

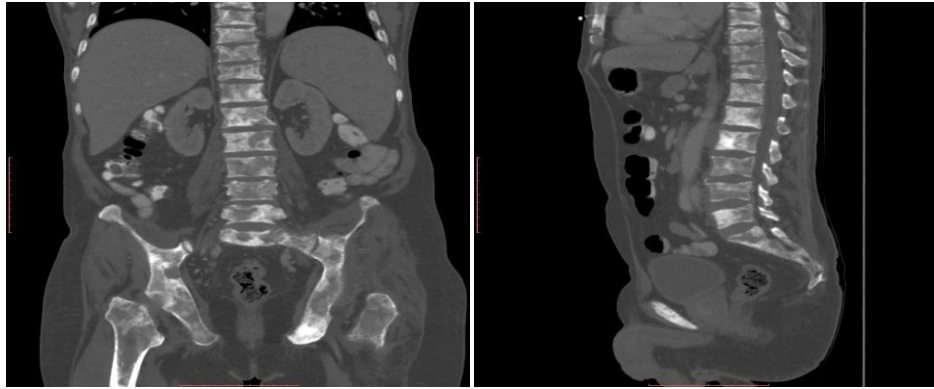


Figure 7a

Figure 7b

Coronal (7a) and sagittal (7b) images in bone window show multiple osteoblastic and osteolytic lesions in vertebral bodies and pelvic bones - suggestive of metastases.

MRI : MRI of LS spine showed diffuse altered marrow signals in lumbar vertebral bodies and sacrum appearing heterogeneously hypointense on T1WI, both hypointense and hyperintense lesions on T2WI appearing hyperintense on STIR - suggestive of mixed osteoblastic and osteolytic bony metastases. Retroperitoneal lymph nodes were also seen (Figure 8).

NUCLEAR BONE SCANS (With Tc-99m): Showed increased radiotracer concentration in skull, bilateral humerus, bilateral ribs, entire spine, bilateral radius, femora & tibia and pelvic bones - suggestive of extensive skeletal metastases (Figure 9).

PROSTATIC BIOPSY: was suggestive of Prostatic Adenocarcinoma (Gleason score 9) with no perineural invasion

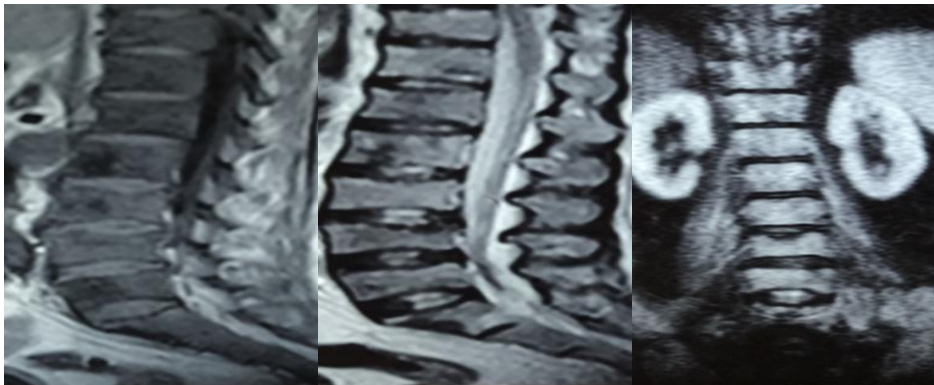


Figure 8a

Figure 8b

Figure 8c

Sagittal T1 (8a), Sagittal T2 (8b), Coronal STIR (8c) MRI of LS spine showing diffuse altered marrow signals in lumbar vertebral bodies and sacrum appearing heterogeneously hypointense on T1WI, both hypointense and hyperintense lesions on T2WI appearing hyperintense on STIR - suggestive of mixed osteoblastic and osteolytic bony metastases.



Figure 9: Nuclear bone scan showed increased radiotracer concentration in skull, bilateral humerus, bilateral ribs, entire spine, bilateral radius, femora & tibia and pelvic bones – suggestive of extensive skeletal metastases.

DISCUSSION

Two lymph node metastatic patterns are recognised in Ca prostate: pattern 1 includes metastases to pelvic and para-aortic lymph nodes and pattern 2 includes metastases to para-aortic lymph nodes only. In Type 1 pattern, the lymph node metastases appear to be continuously invasive and significantly associated with less frequent metastases to the lungs. The Type 2 lymph node metastases are "skip-type metastases" or lymph node metastases. [5]

Haematogenous spread commonly occurs in bones and rarely in lungs, liver, brain, spleen, adrenal glands, kidneys, muscles, pancreas, and salivary glands. Liver, spleen and lungs are atypical metastatic sites of CA prostate.

The lungs are second or third only to bone and/or lymph nodes as metastatic sites from Ca prostate. [2] Incidence of clinically apparent pulmonary metastases at initial diagnosis is 5-27%, whereas autopsy rates show incidence between 23-74%. [5] Pulmonary metastases develop subsequent to other metastatic sites in 1.6% of population and their part of initial pattern of metastases in 2% population. [2] Absence of urinary symptoms might mask the suspicion of Ca prostate as primary adenocarcinoma. Hence, lung lesions mimic metastatic lung cancer or a lymphoma. Rapid and dramatic regression of lung lesions and lymph nodes confirms their metastatic nature and shows androgen deprivation as an effective mode of palliation even for metastatic Ca prostate without bone involvement. [2]

Spleen is the most vascular organ in body but it is an infrequent site of tumour metastases. [6] Proposed mechanism for relative paucity of splenic metastases are: 1. Mechanical factors: (a) The sharp angle made by the splenic artery, which makes it difficult for tumour emboli to enter spleen, (b) Rhythmic contractile nature of the spleen, which squeezes out tumour emboli and prevents their lodging in the spleen, (c) Absence of afferent lymphatics to bring metastatic tumour to the spleen 2. Inhibitory

effect: Antitumor activity due to a high concentration of lymphoid tissue in the spleen (inhibitory effect of splenic micro-environment on growth of metastatic cells). Mechanical factors seem to play a minor role in rarity of splenic metastases. Though implantation of cancer cells in splenic parenchyma may occur, clinically detectable splenic metastases are rare as splenic micro-environment may not facilitate growth of micro metastatic foci. Expression of chemokines in spleen does not constitute obstacle to cancer cell homing as stromal cell derived factor 1; (ligand for CXC chemoreceptor - 4 expressed by various types of metastatic cells) is found in bone marrow, lung, lymph node and also in spleen where it plays as crucial role in lymphocyte homing. [6]

Splenic metastases can present as three main macroscopic patterns: macronodular, micronodular, and diffuse. [2] In macronodular pattern, the splenic parenchyma shows multiple macroscopically solitary or multiple large nodules of varying sizes. In micronodular pattern, spleen shows uniform miliary nodules which are either located in the white pulp or the red pulp. Diffuse pattern is characterised by the complete replacement of the splenic parenchyma by tumour cells. In microscopic pattern, no macroscopic lesion is seen. Tumour cells are confined to red pulp, white pulp, venous sinuses, trabecular vessels or in several of these compartments. Irrespective of pattern of splenic infiltration, both primary tumour and splenic metastasis are similar in terms of cytologic and architectural aspect. Splenic metastases due to haematogenous dissemination are confined to the splenic parenchyma and should not be confused with small superficial subcapsular foci associated with peritoneal dissemination seen in Ca ovary. Hence, incidence of splenic metastases is less. However, now its incidence is increasing due to the improvement of medical imaging and the long-term follow-up of patients with cancer. Solitary metastases in spleen are reported

which is difficult to differentiate from primary tumour of spleen. Splenic metastases occur in a context of multivisceral metastatic cancer at terminal stage.

Breast, lung, ovarian, colorectal, gastric carcinomas and skin melanoma are the most common primary sources. [2] Prevalence of splenic metastases in large population with cancer was obtained from autopsy series published before 1990 and ranged between 2.3% and 7.1%. Largest autopsy series was reported by Berge. [7] In a Japanese study, 0.15% of 24761 patients examined by ultrasonography had splenic metastasis. [8] Splenic metastasis usually constitutes a late manifestation of widespread disseminated metastases in cancer patients in terminal stage. Hence, presence of splenic metastasis is generally considered a crucial sign, indicating an unfavourable outcome. [8]

90% of skeletal metastases are multiple. Breast, lung, prostate and kidney tumours constitute 80% of all bony metastases. Ca prostate constitutes 60% of all bony metastases in men while Ca breast constitutes 70% of bone metastases in women. Ca prostate metastasis is usually purely osteoblastic. They are either multiple, round, well-circumscribed sclerotic lesions or present as diffuse skeletal sclerosis. Prostate cancer is the second most common cancer in men after lung cancer and fifth most common cancer worldwide. Ca prostate frequently metastasizes to bone but metastases can also occur in other body organs and tissues which contribute to morbidity with advanced disease. The pathogenesis of bone lesions in prostate cancer is not well understood. Prostate cancer cells promote both osteolytic and osteoblastic activity through production of factors that have direct and indirect osteogenic properties. Factors like bone morphogenetic proteins, endothelin-1, PSA and parathyroid hormone-related protein promote osteoblastic activity. [9]

Receptor activator of nuclear factor kappa-B ligand (RANKL) and its receptor (RANK) signalling promote osteoclastic activity while osteoprotegerin (OPG) protects the skeleton from excessive bone resorption by binding to RANKL and preventing it from binding to its receptor, RANK. Prostate cancer cells express OPG and RANKL. [10] The RANKL to OPG ratio determines bone mass with a decrease in OPG resulting in excessive bone resorption. In some patients with predominantly osteolytic bone lesions, balance of RANKL to OPG is altered. Hence, rare cases of osteolytic metastases in Ca prostate are reported.

Haematogenous metastases were present in 35% of cases, with bone in 90%, lung in 46%, liver in 25%, pleura in 21%, and adrenals in 13%. There is existence of backward metastatic pathway through veins from the prostate to the spine in addition to classical hematogenous tumour spread via the vena cava. There is inverse relationship between spine and lung metastases, suggesting that metastasis to spine are independent of lung metastasis. Spine metastases precede lung and liver metastases. There is gradual decrease in spine involvement from lumbar to cervical level (97% vs 38%). This is consistent with a subsequent upward metastatic spread along spinal veins after initial lumbar metastases. [3]

CONCLUSION

Multiple splenic metastases in Ca prostate are rare. Apart from retroperitoneal lymphadenopathy, skeletal metastases and direct spread by contiguity, rare sites of metastases by hematogenous spread in spleen, liver and lungs should also be sought for. Splenic metastasis with/without multivisceral involvement occurs in terminal stage of Ca prostate and is thus helps us in prognostification.

REFERENCES

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin

- DM, Forman D, Bray F. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015 Mar 1; 136(5):E359-86.
2. Compérat E, Bardier-Dupas A, Camparo P, Capron F, Charlotte F. Splenic metastases: clinicopathologic presentation, differential diagnosis, and pathogenesis. *Arch Pathol Lab Med*. 2007 Jun; 131(6):965-9.
 3. Bubendorf L, Schöpfer A, Wagner U, Sauter G, Moch H, Willi N, Gasser TC, Mihatsch MJ. Metastatic patterns of prostate cancer: an autopsy study of 1,589 patients. *Hum Pathol*. 2000 May; 31(5):578-83.
 4. Giorgio Gandaglia, Pierre I Karakiewicz, Maxine Sun. Beyond the Bone: Atypical Metastases in Prostate Cancer. *Cancer Cell Microenviron* 2014; 1: e26.
 5. Agha - Mohammadi S, Calne RY. Solitary splenic metastasis: case report and review of the literature. *Am J ClinOncol*. 2001 Jun; 24(3):306-10.
 6. Lam KY, Tang V. Metastatic tumors to the spleen: a 25-year clinicopathologic study. *Arch Pathol Lab Med*. 2000 Apr; 124(4):526-30.
 7. Berge T. Splenic metastases. Frequencies and patterns. *Acta Pathol Microbiol Scand A*. 1974 Jul; 82(4):499-506.
 8. Ishida H, Konno K, Ishida J, Shirayama K, Naganuma H, Komatsuda T, Hamashima Y, Masamune O. Isolated splenic metastases. *J Ultrasound Med*. 1997 Nov; 16(11):743-9.
 9. Segamwenge IL, Mgori NK, Abdallahyussuf S, Mukulu CN, Nakangombe P, Ngalyuka PK, Kidaaga F. Cancer of the prostate presenting with diffuse osteolytic metastatic bone lesions: a case report. *J Med Case Rep*. 2012 Dec 28; 6:425.
 10. Brown JM, Corey E, Lee ZD, True LD, Yun TJ, Tondravi M, Vessella RL. Osteoprotegerin and rank ligand expression in prostate cancer. *Urology*. 2001 Apr; 57(4):611.

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