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Rosette like secondaries of prostatic adenocarcinoma in the inguinal lymph nodes: A rare case presentation

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Abstract
Prostate cancer is among the top ten cancers in India. Approximately half of patients with prostate cancer have metastasis on presentation, bones and regional lymph nodes being most common. A case of metastasised cancer of prostate presenting only with an inguinal mass without any other symptom is rare.

Keywords: prostate, adenocarcinoma, metastasis, rosette, inguinal

Introduction
Prostatic adenocarcinoma is the most common cancer in males and approximately 50% of patients have metastases at presentation, most commonly spreading to the bones and regional lymph nodes [1]. It usually spreads by direct, lymphatic and haematogenous dissemination. It spreads to the prostatic capsule, bladder base and seminal vesicles by direct invasion. Lymphatic spread usually occurs to the external and internal iliac, obturator, presacral and hypogastric nodes, and then to para-aortic lymph nodes [2]. Prostate cancer metastasising to inguinal lymph nodes in the absence of pelvic lymphadenopathy or other metastases is very uncommon.[1]
Gleason grading pattern 4 is poorly formed glands include small nests of cells with only a rudimentary formed luminal space almost rosette like.[3] Clinically, when small cell carcinoma metastasizes it may be difficult to determine the origin of the small cell carcinoma. In some cases, there is no history of usual adenocarcinoma of the prostate, and as we have demonstrated serum PSA levels are often not elevated. In metastatic sites, especially in the absence of concurrent usual prostatic adenocarcinoma, prostate-specific immunohistochemical markers may be helpful in identifying the lesions as being of prostatic origin. P501S and PSMA were better in identifying the prostatic origin of small cell carcinoma than PSA. As small cell carcinoma of the prostate is treated with chemotherapy, as opposed to advanced usual adenocarcinoma of the prostate that is treated with hormonal therapy.[4] Metastatic prostatic adenocarcinoma commonly involves the axial skeleton and the regional lymph nodes [5]. Pure small cell neuroendocrine carcinomas of the prostate are slightly more common than mixed small cell adenocarcinomas. Larger atypical cells, formation of true rosettes or pseudo-rosettes, and a large clear and vacuolated cytoplasm are also described.

Case report
A 65-year-old male presented with a left inguinal swelling for 2 months and pain over swelling since 1 month. He had history of weight loss and anorexia since 2 months with increased frequency of micturition at night since 1 month. Local examination revealed a single, firm, fixed left inguinal swelling of 4 x 4 cm with left cervical lymphadenopathy. USG [Ultrasonography] report was suggestive of left inguinal hernia. FNAC [Fine needle aspiration cytology] study was done and revealed [Fig.1A,B] cellular smears with cells arranged in rosette or acinar pattern in the background of proteinaceous fluid. Cytologically opined as secondaries from epithelial malignancy with a differential diagnosis of neuroendocrine tumour and excision biopsy was advised.

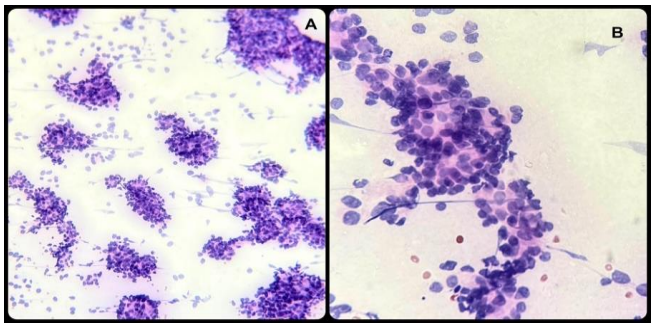

Fig 1: FNAC left inguinal mass: [A]: cellular smears with cells arranged in rosette or acinar pattern in the background of proteinaceous fluid. [PAP; A:10X; B: 40X]

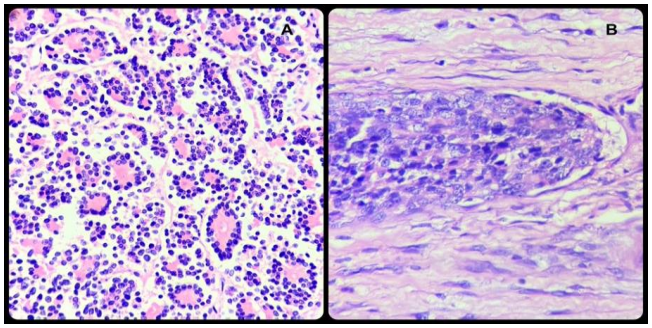

Fig 2: Photomicrograph showing: [A]: Lymph node totally replaced by tumour tissue composed of diffusely arranged small cells with rosette formation with fibrillary matrix in the centre. [H&E:10X] [B]: Vascular invasion of the tumour tissue in the para lymphatic vessel. [H&E: 40X]

Patient was operated for left inguinal hernia and biopsy of the inguinal mass was done. Histologically revealed [Fig. 2; A, B] a lymph node totally replaced by tumour tissue composed of diffusely arranged small cells with rosette formation with fibrillary matrix in the centre admixed with areas of necrosis. Para lymphatic vessels showed vascular invasion of the tumour tissue.

On IHC [immunohistochemistry], the tumour showed immunopositively for pan cytokeratin (AE1/AE3), PSA, AMACR, NKX3.1 and immunonegative for TTF1, Pax 8, and thyroglobulin. Hence diagnosis of metastatic adenocarcinoma from prostatic in the left inguinal lymph node was confirmed on IHC.

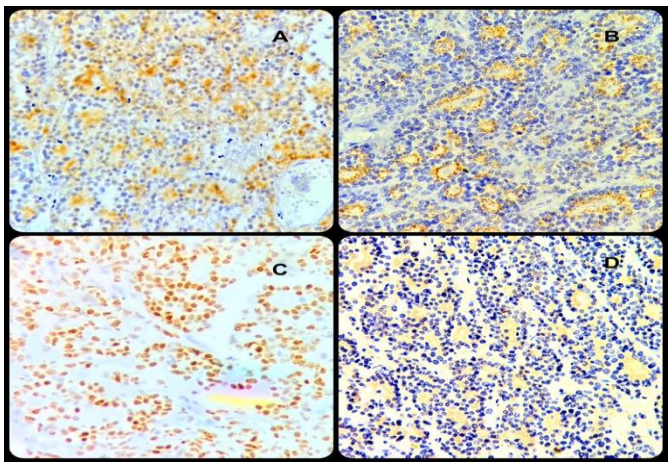

Fig 3: Photomicrograph showing tumor cells immuopositive for: [A]: PSA, [B]: AMACR [C] NKX 3.1and [D]PAN CK (AE1, AE3) [H&E: 40X]

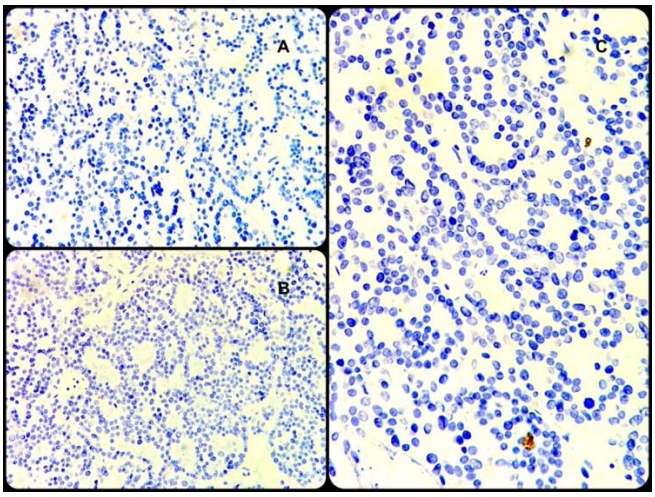

Fig 4: Photomicrograph showing tumor cells immuonegative for: [A]: Thyroglobulin, [B]: PAX- 8 and [C]TTF-1 [H&E: 40X]

Discussion

Prostatic adenocarcinoma is the most common tumour in males, accounting for approximately 3.4% of all the cancers, and is the second most common cause of cancer-related death in males. Approximately 50% of patients have metastases at presentation, most commonly spreading to the bones and regional lymph nodes [1]. Prostatic adenocarcinoma usually spreads by direct, lymphatic and haematogenous dissemination. Inguinal lymphadenopathy in the absence of pelvic lymphadenopathy is very rare as like in our case.

Jackson et al. reported that 9% of patients presenting with pelvic nodal enlargement had inguinal lymph node metastasis. Postoperatively, inguinal lymphadenopathy may arise due to preoperative aberrant lymphatic drainage of prostate and postoperative distortion of the lymphatic drainage. It is also possible that malignant cells can reach the inguinal nodes via spermatic cord through localised spread or from ectopic prostate tissue outside the genitourinary system [1]. Usually, prostate cancer spreads primarily to the regional lymph nodes and bones, followed by lung, bladder, liver, and adrenal gland [3].

Our case presented with small cells/ oat cells arranged in rosette like secondaries in the inguinal nodes. The differential diagnosis of small cells/ oat cells with or without rosette formation with secondaries in the inguinal nodes must include small cell carcinoma of lung, small cell carcinoma of prostate, neuroendocrine carcinoma, poorly differentiated prostatic adenocarcinoma and the extremely rare carcinoid tumour.

Classic oat cell morphology consists of tumour cells with scant cytoplasm and round, oval, or spindled nuclei usually smaller than 3 times the size of lymphocytes with fine granular chromatin, and absent or inconspicuous nucleoli. This subdivision of small cell carcinoma into oat cell and intermediate cell types, as initially proposed in the 1981 World Health Organization classification of lung carcinomas.

Neuroendocrine [NE] differentiation comprises a spectrum ranging from NE-differentiated cells in normal prostatic epithelium to focal NE differentiation of various extent in usual adenocarcinomas as well as NE small-cell carcinomas (SCC) and the extremely rare carcinoids both reflecting pure NE tumours of the prostate [8].

Some of the small cell carcinomas of the prostate have morphologic features that could be more readily confused with usual poorly differentiated adenocarcinoma of the prostate. A comprehensive immunohistochemical panel to differentiate small cell carcinoma from poorly differentiated adenocarcinoma includes PSA, PSAP, P501s, and neuroendocrine markers, CD 56 being the most sensitive for small cell carcinoma. TTF-1 can be positive in up to half of small cell carcinomas and is not found in the poorly differentiated adenocarcinomas. Most small cell carcinomas are negative for the aforementioned prostate markers (PSA, PSAP, and P501S). Poorly differentiated adenocarcinomas are usually diffusely positive for the same antibodies. Expression of neuroendocrine markers can be seen in conventional acinar adenocarcinomas, and the diagnosis of neuroendocrine carcinomas should rely in both immunohistochemical profile and light microscopic morphology.

Small cell carcinomas can be positive (even focally) for at least one prostatic marker (PSA, PSMA, PSAP, or P501s) which are not expressed in lung tumours. CD44, a cell-surface molecule proposed to identify cancer stem/progenitor cells in prostate cancer, has been demonstrated to be highly specific of small cell carcinoma of the prostate. Conventional adenocarcinoma do not show CD44 positivity and have expression of PSA and androgen receptors like LNCaP, another known cell line associated with prostatic carcinoma.[9] Small cell carcinoma had rosette formation seen in 29% of cases consisted of both true and pseudorosettes [4]. TTF-1 cannot be used as a marker to distinguish between lung and prostatic origin of small cell carcinoma.

As the prostate specific markers like PSA, AMACR, NKX-3 and also PAN CK (AE 1, AE 3) were immune reactive in our case, we confirm our case to be of Adenocarcinoma prostate metastasis to inguinal nodes.

Conclusion

Presentation of prostatic carcinoma with inguinal mass is rare as they usually present with iliac nodes or bony metastasis. Patients presenting with inguinal lymphadenopathy should be dealt with high clinical suspicion as they are already in advanced stages of the disease process.[2] Pelvic and abdominal retroperitoneal lymph nodes are the most common sites of adenopathy in prostate cancer. Any lymphadenopathy occurring outside the abdomen and pelvis is considered atypical.[6] In such cases, the diagnostic difficulty is aided by immunohistochemical staining of lymphatic biopsy, prostatic biopsy, and serum PSA testing [5].

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