CASE REPORT

Cervical Lymphadenopathy as a Presentation of Prostate Adenocarcinoma: A Case Report.

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ABSTRACT

Lymph node involvement of prostate adenocarcinoma typically involves regional locations. Distant sites, particularly the cervical region, are rare. We report an unusual case where a 77-year-old man was incidentally found to have left cervical lymphadenopathy during a routine clinic visit. Fine needle aspiration cytology revealed numerous monomorphic cells with inconspicuous nucleoli, prominent smear artefact and occasional acinar formation, set within a clean background. Metastatic carcinoma from several different sites were considered as the differential diagnoses, including adenocarcinoma of nearby organs, small cell carcinoma and poorly differentiated squamous cell carcinoma, among others. Positive immunohistochemistry for PSMA confirmed prostate origin, while negativity for CK7, CK20, CK5/6, TTF-1, chromogranin A and synaptophysin ruled out other differential diagnoses. This case highlights the diagnostic utility of cytological examination in identifying occult metastases and underscores the importance of considering rare sites of primary malignancy in such cases, even in the absence of typical clinical presentations.
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INTRODUCTION

Prostate cancer is among the most common malignancies affecting adult males, with incidence increasing significantly after age 55 and peaking in the eighth decade of life. Clinical presentations vary - many patients are asymptomatic and diagnosed based on elevated serum prostate-specific antigen (PSA) levels, while others present with advanced disease. The most common metastatic sites include regional lymph nodes (obturator, internal/external iliac, presacral, and para-aortic), followed by bone, lungs, liver, brain, and epidural space. Metastases to non-regional lymph nodes such as the mediastinum, retroperitoneum, and supraclavicular regions are rare. We report a rare case of metastatic prostate cancer presenting initially with left supraclavicular lymphadenopathy in a 77-year-old man, previously undiagnosed with prostate disease. This case illustrates the diagnostic value of fine needle aspiration cytology (FNAC) in such atypical presentations.

CASE REPORT

A 77-year-old man under dermatological follow-up for tinea corporis was noted to have multiple swellings on the left side of his neck. He reported recent weight loss and decreased appetite but denied fever, night sweats, chronic cough, changes in bowel habits, or contact with tuberculosis. On examination, multiple hard, non-tender left cervical lymph nodes were noted, the largest measuring 1.5 cm × 1.0 cm × 1.0 cm. An FNAC was performed; however, neck ultrasound and tumour marker tests were not done at that time.

Cytology smears showed high cellularity, with tumour cells in flat cohesive sheets, displaying marked smear artefact. Vague acinar structures were seen. The cells were monomorphic, with hyperchromatic, round nuclei, inconspicuous nucleoli, and scant cytoplasm. Some cells showed nuclear moulding. Notably, the background was clean, lacking the expected lymphoid elements from a lymph node aspirate. The cell block showed similar tumour morphology with cribriform architecture.

Immunohistochemistry examinations were positive for CKAE1/AE3 and PSMA. The tumour cells were negative for CK7, CK20, CK5/6, TTF-1, Synaptophysin and Chromogranin A. He was diagnosed with metastatic prostate adenocarcinoma.

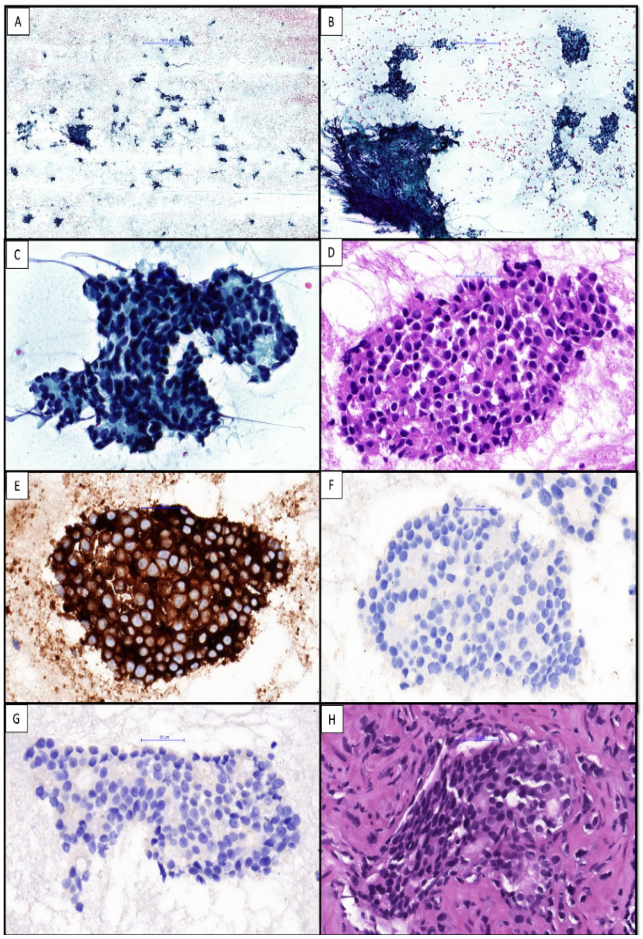

Fig. 1: (A) The smear was cellular and set within a clean background (Papanicolaou stain, 20x). (B) The tumour cells showed prominent smear artefacts (Papanicolaou stain, 100x). (C) The tumour had monomorphic nuclei with scanty cytoplasm, indistinct cell borders and acinar formation (Papanicolaou stain, 400x). (D) Cell block highlighted the acinar pattern (Haematoxyoin and eosin stain, 400x). (E) The tumour cells showed diffuse positivity for PSMA immunohistochemistry (400x). (F) and (G) The tumour cells were negative for TTF-1 and synaptophysin immunohistochemistry, respectively (400x). (H) Histopathological examination of the prostatic biopsy revealed malignant glands exhibiting monomorphic nuclei with cribriform structure (Haematoxyoin and eosin stain, 400x).

Following this diagnosis, a serum PSA test was conducted, revealing a significantly elevated level of 467 ng/ml. Digital rectal examination revealed a firm to hard prostate gland. Transrectal ultrasound guided prostate biopsy showed diffuse acinar adenocarcinoma involving bilateral apices, mid glands and bases, with Gleason score 8 to 9, WHO/ISUP Grade Group 4 to 5 and presence of perineural invasion. Subsequent bone scan revealed multiple hydroxymethylene diphosphonate (HDP)- avid lesions in the axial and appendicular skeleton in keeping with extensive bony metastases. He was started on androgen deprivation therapy (ADT).

DISCUSSION

Cervical lymph node enlargement is a common presentation for metastatic carcinoma, most associated with malignancies originating above the diaphragm - particularly from the head and neck mucosa - followed by non-mucosal sites like the salivary glands, thyroid gland, and skin. In contrast, prostate adenocarcinoma tends to metastasise to bone and regional lymph nodes. Supradiaphragmatic lymph node involvement, particularly at presentation, is uncommon in prostate adenocarcinoma, occurring in fewer than 0.5% of cases (1, 2).

Cytological Features of Prostate Adenocarcinoma

The rarity of this entity leads to limited familiarity with its cytomorphological features among pathologists. Key cytological characteristics of prostate adenocarcinoma seen in this case include tight microacinar architecture and a clean background. Other features such as oval to round nuclei and poorly defined cell borders were also present, but these findings were nonspecific as they could be seen in many poorly differentiated tumours. Interestingly, most prostate adenocarcinomas cells are described as having prominent nucleoli; however, in our case, the nuclei were hyperchromatic with mostly indiscernible nucleoli. These features were also observed in the cell block and tissue biopsy.

Differential Diagnoses

Given the location of the lymph node and the presence of acinar formation, carcinomas from other organs - such as the thyroid, lung and gastrointestinal tract - were initially considered. The cells of prostate adenocarcinomas are uniform and monomorphic, in contrast to typical adenocarcinomatous cells, which often have large, pleomorphic nuclei, vesicular chromatin and large, cherry-red nucleoli. The lesional cells lacked the nuclear features of papillary thyroid carcinoma and the microfollicles of thyroid follicular carcinoma. Small cell neuroendocrine carcinoma was also actively considered, particularly given the hyperchromatism, scant cytoplasm, smear artefact and occasional nuclear moulding. Although acinar patterns may occasionally be seen in neuroendocrine carcinoma, their cells are typically less cohesive, show coarse salt and pepper chromatin, and are associated with a dirty background due to necrosis. Other differential diagnoses considered – though with lower suspicion - include poorly differentiated squamous cell carcinoma, malignant melanoma and lymphoma (Table I). Adequate cellularity on the cell block and ancillary diagnostic tools such as an extensive immunohistochemistry panel, are essential for accurate interpretation.

Table I: Cytological features of metastatic prostatic adenocarcinoma in comparison to other differentials.

Cytological features	Prostate adenocarcinoma	Small cell carcinoma	Squamous cell carcinoma	Melanoma	Lymphoma
Smear cellularity	Moderate	High	Variable	High	High
Shapes of cell fragments	Cohesive clusters with smooth external border, single cells	Individual cells or loosely cohesive clusters, crush artifact.	Sheets, large clusters or single cells.	Discohesive cells with scattered singly distributed cells.	Hyperchromatic lymphoid clusters Evenly distributed monotonous population.
Cellular features	Uniform and small with a high nuclear to cytoplasmic ratio. The cytoplasm is scanty with indistinct cytoplasmic borders. The nuclei are round-to-oval, typically with prominent nucleoli.	Small cells (twice the size of lymphocytes) with scant cytoplasm, nuclear molding, fine dispersed, chromatin, and small to indistinct nucleolus.	Differs depending on the degree of keratinization of the tumour. The cytoplasm is usually dense and occasionally orangeophilic. Nuclei are enlarged, hyperchromatic, and coarsely granular; nucleoli are usually not prominent.	Epithelioid, spindle or pleomorphic shapes. Cells with eccentric nuclei, macronucleoli, nuclear inclusions. Variable intracytoplasmic melanin pigment. Binucleation or multinucleation.	Small to large lymphoid cells with variable chromatin and nucleoli. Pleomorphic cells in some subtypes.
Background	Clean or inflammatory	Necrotic debris and apoptotic cells	Necrotic debris	Melanin pigment, bloody or necrotic background	Mixed inflammatory cells (lymphocytes, eosinophils, histiocytes), lymphoglandular bodies, or epithelioid histiocytes.
Immunohistochem-ical stains	PSA, NKX3.3, AMACR, PSMA.	Synaptophysin, Chromogranin-A, CD56.	p40, p63.	SOX10, S100, Melan-A, HMB45.	CD45, B and T cell markers.

Mechanisms of Metastasis to Cervical Lymph Nodes

Two primary hypotheses attempt to explain the spread of prostate cancer to the supraclavicular lymph nodes. One theory suggests hematogenous dissemination through the vertebral venous plexus (Batson's plexus), which would be expected to result in equal involvement of both sides of the neck. However, prostate adenocarcinoma more commonly affects the left side, as seen in our case.

A more compelling explanation involves lymphatic spread. Prostate cancer typically follows a predictable lymphatic route: tumour cells initially spread to the obturator, hypogastric, and presacral lymph nodes, then to the cisterna chyli via the iliac and para-aortic nodes and subsequently progress to the cervical lymph nodes through the thoracic duct. Entry into the systemic circulation then occurs via the left subclavian vein (3, 4).

Clinical Implications

Cervical lymph node metastasis in prostate adenocarcinoma indicates an advanced disease. Survival outcomes vary, but generally, patients face poor prognosis with mean survival ranging from 12 to 34 months following diagnosis. This underscores the importance of timely diagnosis and intervention to improve outcomes (5). Overall, recognising these rare metastatic patterns and employing a multidisciplinary diagnostic approach are crucial for accurate diagnosis and effective management of advanced prostate cancer.

CONCLUSION

This case highlights a rare but important presentation of metastatic prostate adenocarcinoma to a cervical lymph node, specifically the left supraclavicular region. FNAC proved to be a valuable diagnostic tool in this atypical scenario. A high index of suspicion, combined with cytomorphological analysis and appropriate immunohistochemical workup, is essential to accurately identify such rare metastatic patterns. Clinicians should consider prostate cancer in the differential diagnosis of supraclavicular lymphadenopathy, even in the absence of typical lower urinary tract symptoms.

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