Small cell carcinoma of prostate

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ABSTRACT

Small cell carcinoma(SCC) of prostate is a very rare and highly aggressive neoplasm which constitutes less than 1 % of all prostate cancers. Half of the small cell carcinomas arising in the prostate are pure without an associated adenocarcinoma. Majority of SCC of prostate present at the advanced stage of disease and a disproportionately low serum PSA levels as compared to adenocarcinoma prostate. Chemotherapy and associated surgery are mainstay of treatment along with palliative radiation. Due its very poor prognosis and high mortality, it is necessary to diagnose it early and treat aggressively.

Keywords: Small cell carcinoma, Prostate, Prostate specific antigen, Neuroendocrine tumour

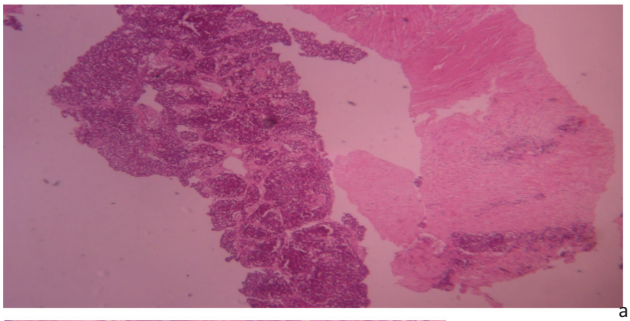
INTRODUCTION

Small cell carcinoma (SCC) is a rare high grade epithelial neoplasm of the prostate with an incidence rate of about 0.35 cases per million per year and 59 % occur in men 70 years and above[1]. These tumors may originate from many different parts of body including larynx,esophagus,urinary bladder and urogenital system[2] . Patients with this aggressive disease have frequent visceral metastases and less often paraneoplastic syndromes such as those associated with ectopic adrenocorticotrophic hormone, hypercalcemia, or inappropriate antidiuretic hormone production[3] . In contrast to most prostatic adenocarcinomas, the small cell variant does not usually secreate prostate-specific antigen (PSA) and often cause lytic bone lesions[4] . Five year and median overall survival for prostatic small cell carcinoma are the lowest among prostate cancer subtypes at 12.6% and 10 months respectively[5]. Extra pulmonary small cell carcinoma of prostate is very rare. We report a case of pure small cell carcinoma of prostate with seminal vesicle invasion .

CASE REPORT

A 56 year old male patient presented to the emergency department with acute urinary retention for one week. He was treated at a primary health centre for acute urinary tract infection with a per-urethral catheter. Digital rectal examination detected a prostate gland larger and firmer than normal, strongly suspicious of a neoplasia. A serum PSA was ordered and found to be 52.91 ng/ml. Serum creatinine was 0.6 mg/dl; Alkaline phosphatase was 96.0 U/L; Aspartate amino transferase 41.0 U/L; Alaninine amino tranferase 57.0 U/L. The patient was scheduled for transrectal ultrasound(TRUS) which showed an enlarged prostate gland of 135 cc. CT Scan of the prostate showed a tumour which measures 74 mm x 14 mm. The MRI showed seminal vesicle invasion. A TRUS guided prostate needle biopsy was taken and submitted for histopathological examination. The histological evaluation revealed the presence of small cell carcinoma without any associated adenocarcinoma. Immunohistochemistry confirmed the diagnosis with chromogranin + and CD 56+ . Later a serum Chromogranin was ordered and found to be raised with a value of 208.9 ng/ml. A bone scan was performed and found to be negative. The patient is being treated with chemotherapy : Cisplatin and Etoposide.

Figure 1a & 1b: Three of the six core needle biopsies of prostate showed a small cell carcinoma with homogenous population of blue cells with round nuclei and a salt - and-pepper chromatin(H&E,100X,400X)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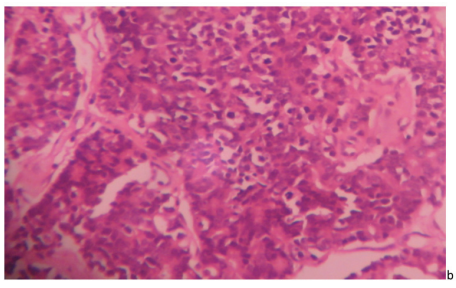
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DISCUSSION

Neuroendocrine carcinoma are rare outside the lung. Approximately 10 % cases occur in the prostate, making it one of the most common extrapulmonary sites[6] . The current World Health Organization (WHO) histologic classification of neuroendocrine tumors of the prostate which is based solely on microscopic histomorphology and immunohistochemical studies and includes (1) Focal NE differentiation in conventional prostate adenocarcinoma;(2) Carcinoid tumor(WHO well-differentiated NE tumor; and (3)Small cell NE carcinoma(WHO classification, poorly differentiated). The classification based solely on microscopic, histomorphology and immunohistochemical studies[3] . Morphologic variations of small cell carcinoma include: intermediate cell type with slightly more open chromatin and visible small nucleoli seen in about 30- 40 % of cases[3] . SCC of prostate may occur in pure form(50-60%) of cases, but it may also occur adjacent to or concomitantly with conventional adenocarcinoma in other 40-50% of cases[1] . Our case is a pure SCC of prostate without adjacent adenocarcinoma.

Patients with SCC of the prostate most frequently present with voiding symptoms, neurological symptoms (such as confusion and sensory motor deficits), or constitutional symptoms. Given its proclivity to release ectopic peptides, SCC of the prostate has also been associated with paraneoplastic syndromes such as Cushing syndrome, hypercalcemia, Eaton-Lambert syndrome, and syndrome of inappropriate antidiuretetic hormone(SIADH). Unique features of SCC include unresponsiveness to hormonal therapy, rapid progression, increased risk of lytic bone lesions, presence of visceral metastases, markedly enlarged prostate and disproportionately low serum PSA levels[7] .

The histologic features of SCC of the prostate include small tumor cells with minimum cytoplasm, indistinct cell borders, nuclear moulding, fine salt-and –pepper chromatin, lack of prominent nucleoli, extensive tumor necrosis, apoptosis, high mitotic rate and nuclear fragility. Immunohistochemically, SCC of prostate show strong chromogranin and synaptophysin positive expression in the majority of cases(61 % and 89 %); 17 % and 24 % of cases are positive for PSA and PSAP; 24 % and 35 % of cases are positive for basal cell markers, P63 and HMWCK respectively[1] . In a study of 95 cases of Prostatic small cell carcinoma, neuroendocrine markers were positive in 94% of tumors and CD 56 was found to be the most sensitive marker[5].

In SCC of prostate as the small cell component predominates, the PSA and Prostatic acid phospatase (PAP) level falls, where as in combined adenocarcinoma and SCC of prostate, the PSA and PAP levels are elevated[8,2] . In our case the Serum PSA level was 52.91 ng/ml,which is highly elevated probably due to urinary tract retention and prolonged urethral catheter insertion. In SCC of prostate the serum chromogranin levels are elevated . In our case the serum Chromogranin level was 208.9 ng/ml,which is highly elevated.

Because of the rarity of the primary SCC of prostate, it is important to exclude a metastasis from other sites such as urinary bladder. Fluorescence in-situ hybridization (FISH) or reverse transcription polymerase chain reaction(RT-PCR) of fusion gene ERG(ETS-related gene) and TMPRSS2 are important techniques to distinguish primary small cell carcinoma of prostate and metastasis from other sites. Small cell carcinoma is positive for TMPRSS2- ERG fusion gene by FISH. Newer studies looking for molecular targets are Aurora kinase(AURKA) amplification and MYCN proto-oncogene overexpression etc [5] .

The treatment of small cell carcinoma of prostate is a multimodality approach with chemotherapy as the main stay of treatment, and radiation as supplemental for local control or for palliation. Regimens that usually used include Gemcitabine, Docetaxel and Carboplatin , or Cisplatin. However, primary surgery that include radical prostatectomy was the most important prognostic factor for prolonged survival in one study [6] . Prognosis of SCC of prostate is poor for its extreme aggressiveness and frequent metastatic potential.

CONCLUSION

Primary SCC of prostate is a very rare and aggressive malignant tumor with frequent metastasis at the time of presentation. No standard therapeutic regimen exists for primary SCC of prostate and the predicted survival is very short. A combined clinical, radiological, biochemical, histomorphology and immunohistochemical approach is required for diagnosis. Clinician should attempt to diagnose it early and treat aggressively with multimodality approach to improve survival.

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