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Case Report

SMALL CELL NEUROENDOCRINE CARCINOMA OF PROSTATE, A CASE REPORT AND REVIEW OF THE LITERATURE

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ABSTRACT

Pure small cell carcinoma of the prostate is a rare and aggressive neoplasm with poor prognosis. Only few cases had been reported in literature and mean survival is 5 months. We reported a case 68-year-old male patient presented with dysuria, and difficulty during urination of about 2-months duration. The prostatic core needle biopsy result was reported as pure small cell neuroendocrine carcinoma and immunohistochemical examination was conformed the diagnosis. Further evaluation showed locoregionally advanced with asymptomatic bone metastasis. He received six cycle of palliative chemotherapy with bone stabilizing agent followed by radiotherapy to locoregional area and responded well.

Keywords: *Immunohistochemistry, Neuroendocrine, Prostate, Small Cell*

INTRODUCTION

Extrapulmonary small cell carcinoma is rare. These tumours may originate from many different parts of the body including gastrointestinal tract, genitourinary tract, the head and neck region, and the unknown primary (Walenkamp *et al.*, 2009). Small cell neuroendocrine carcinoma of prostate (SCNCP) is rare and has a poor prognosis. To our knowledge, 20 cases of pure SCNCP have been described in literature till 2006 (Ketata *et al.*, 2006). High aggressiveness, poor prognosis, and extensive disease are common features of presentation. We report a case of pure SCNCP with locoregionally advanced and asymptomatic bone metastasis at the time of diagnosis.

CASES

A 68-year-old male patient presented with lower urinary tract symptoms of 6-months duration with history of slowness of urine since last 3 years. Digital rectal examination detected a hard nodular enlargement of prostate more towards right side, strongly suspicious of neoplasia. There was no bony tenderness all over the body. Total PSA was 0.92 ng/ml. MRI of pelvis showed a heterogeneous lesion in right peripheral zone with extension into periprostatic space and neurovascular bundles appear to be involved, with right internal iliac (30X25mm in size) and external iliac (15X14mm in size) lymphadenopathies seen. Contrast-enhanced CT scan (CECT) of abdomen and pelvis showed gross enlargement of prostate of 117cm^3 with heterogeneous enhancement and the heterogeneous mass of prostate is invading base of the urinary bladder causing irregular thickening of it, also invading perirectal fat, with extracapsular extension and iliac lymphadenopathies (figure 1). Bone scan showed increase tracer uptake in cervical, thoracic, and both sacro-iliac joints (figure 2). CECT scan of chest ruled out lung metastasis. Trans-rectal ultrasound guided 12 core biopsy from prostate was done. Microscopy revealed multiple cores of needle biopsy tissue of prostate with foci of infiltrative neoplasm composed of round to oval tumour cell with pleomorphic htyperchromatic nuclei, fine granular chromatin, inconspicuous nucleoli and scanty cytoplasm, arranged in sheets. Large areas of necrosis with frequent karryorhctic debris are seen. Mitosis is frequent. Focal lympho-vascular invasion by tumour cells are seen. Immunohistochemistry revealed diffuse strong positivity for CD56, chromogranin A and moderate

intensity positivity in predominant areas for synaptophysin (figure 3). Therefore, it was diagnosed as pure SCNCP.

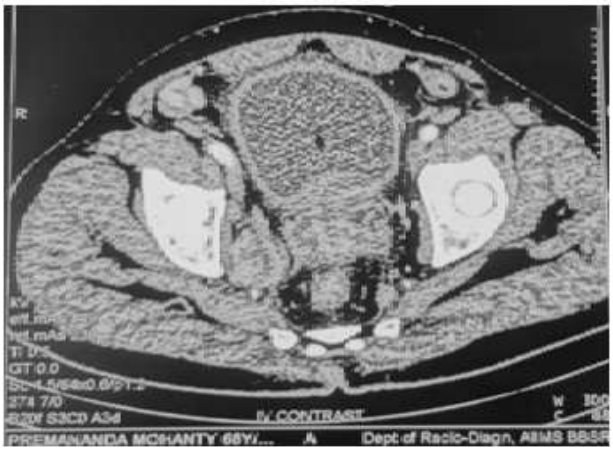

Figure 1: Contrast-enhanced CT scan of abdomen and pelvis showed gross prostate enlargement with heterogeneous prostatic mass invading base of the urinary bladder and a right internal iliac lymphadenopathy

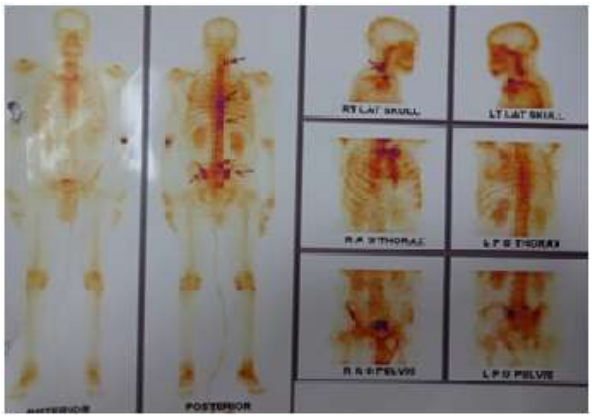

Figure 2: Bone scan showed increased tracer uptake in cervical, thoracic and bilateral iliac bones

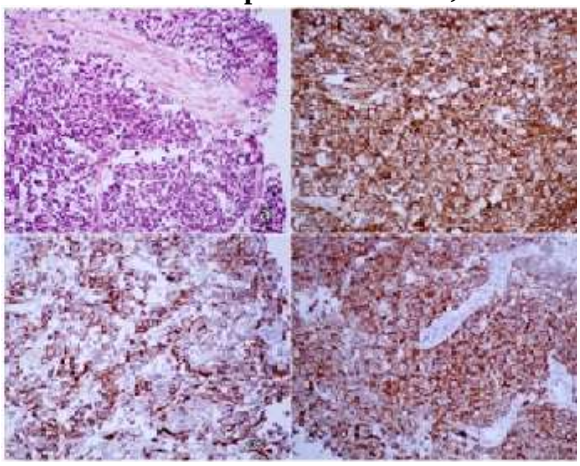

Figure 3: There are presence of Small cell morphology of the tumour cells in left upper half (H&E – 20X), diffuse strong positivity of CD56 Ab in tumour cells in right upper half(CD56, 20x), granular Synaptophysin positivity in majority of tumour cells seen in left lower half (Synaptophysin, 20X), and diffuse strong positivity demonstrated by Chromogranin A in right lower half (Chromogranin A, 20X)

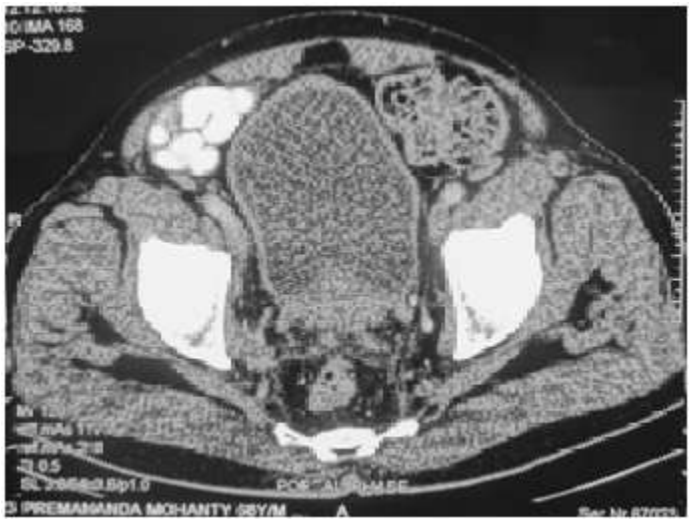

Figure 4: CECT scan showed significant decrease in size of prostatic mass and right internal iliac node

He received four cycles of chemotherapy of etoposide and cisplatin, with bone stabilizing agent zolendronic acid 4mg. Patient responded well to treatment with decrease in urinary symptoms. After four cycles of chemotherapy, CECT scan revealed significant decrease in size of both primary lesion and lymph nodes (figure 4). He was completed six cycles of chemotherapy and followed by radiotherapy to the loco-regional area. He responded well to treatment and tolerated well with manageable toxicity.

DISCUSSION

Small cell carcinomas are heterogeneous and show neuroendocrine differentiation. Of these 20% of patients present with small cell carcinoma in association with a regular adenocarcinoma, 30% during the course of progression of a regular adenocarcinoma, and the remaining 50% presents with pure small cell carcinoma (YU *et al.*, 1990). Small cell carcinoma of the prostate arises from pleuripotent prostatic epithelial cells and may have potential for divergent differentiation into neuroendocrine and acinar tumour cells.

The clinical features of prostatic small cell carcinoma differ from those of adenocarcinoma of the prostate in that it has a predilection to produce visceral metastases, lytic bony lesions, and low amounts of serum prostate-specific antigen (PSA) (Amato *et al.*, 1992). Pure SCNCP is an extremely rare disease with different presentations. Median age of patients is 65 years and prognosis is poor, with a mean survival of 5 months (Wenle *et al.*, 2008). Complete remission was achieved in a few cases (Ishizu *et al.*, 2002). It clinically behaves like small cell carcinoma of the lung. Patients frequently presents with symptoms of prostatisms. Presenting symptoms may be related to metastases and rarely to paraneoplastic syndromes.

Immunohistochemical staining tests such as synaptophysin, chromogranin, neuron-specific-enolase and CD56 are used for SCNCP (Wenle *et al.*, 2008). We made the diagnosis of SCNCP from prostatic core needle biopsy and IHC. IHC revealed positive for CD56, chromogranin A and synaptophysis, and was conformed the diagnosis of SCNCP.

SCNCP is a tumor with a tendency to systemically metastasize. Even at the time of diagnosis, nearly 75% of patients are at advanced stage. It most commonly metastasizes to the lymph nodes, liver, bone, lungs, pericardium, brain, rectum, and urinary bladder (Tetu *et al.*, 1987). Pure SCNCP cases have normal levels of PSA and prostatic acid phosphatise (PAP). In the present case, the total PSA was 0.92ng/ml.

As the number of cases so far is limited, optimal therapy for SCNCP has still to be defined. Extrapulmonary small cell carcinomas are less sensitive to chemotherapy than pulmonary small cell carcinomas. But, our case responded well to chemotherapy. Optimal treatment for SCNCP is still

uncertain. Radical prostatectomy should be performed if the tumour is confined to the prostate. In pure SCNCP hormone-depletion therapy should be avoided, since the androgen receptor is not expressed by the malignant neuroendocrine cells (Ishizu *et al.,* 2002). Cisplatin and Etoposide-based chemotherapy is the standard of care (Sandhu *et al.,* 1997). Radiation therapy may be considered for palliative care (Shamelian and Nortier, 2000).

Our case was diagnosed as SCNCP locoregionally advanced with asymptomatic bone metastasis. We treated the patient with six cycles of chemotherapy (etoposide 100mg/m^2 and cisplatin 30mg/m^2) and bone stabilizing agent (zolendronic acid) followed by locoregional radiotherapy. Patient responded well to treatment.

Conclusion

As pure SCNCP are rare, no standard therapeutic regimen exists and the predicted survival is very short. It seems that intense systemic chemotherapy and radiotherapy lengthen the remission period and increase the survival time. In our case, patient responded well to chemotherapy. So, systemic chemotherapy with etoposide and cisplatin may be the treatment of choice in the metastatic SCNCP. But due to its rarity, there is no standard treatment protocol for pure SCNCP till date and needs further case study for it. Due to aggressive nature of the disease, the case needs close follow-up after completion of treatment.

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