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Small Cell Prostate Cancer; Center Review of Two Cases and Testimony of a Rare and Aggressive Disease

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Abstract

Small cell cancers were initially described in the lungs and later found to occur in a wide range of organs of the body, constituted a disease entity that is characterized by an aggrieve path/course and a huge disease related mortality. They are also called neuroendocrine tumors with peculiar histologic and biologic disease entity. Here we present two cases of small cell cancer of the prostate seen and managed in our facility with focus on their presentation, disease progression and outcome. The first patient was a 72-year-old retired military officer who presented with a progressively painful scrotal swelling of 3-month duration, and scrotal ulceration with contact bleeding of a month duration associated with a foul-smelling discharge. There was also history of progressive weight lost, loss of appetite and constipation. Patient was pale and lethargic on examination with a foul smelling exophytic scrotal mass. Serum PSA was 4 ng/l (within normal limit). Wedge biopsy and trucut prostate biopsy revealed small cell cancer of the prostate. Patient was resuscitated and prepared for chemoradiation, had a single dose of chemotherapy and died before the second dose. Second patient was a 63-year-old farmer who presented with lower urinary tract symptoms, progressive weight loss and constipation of two months duration, a known hypertensive and diabetic who has been regular on his medication. He was lethargic on examination, pale and unable to stand without support. Trucut prostate biopsy shows small cell cancer of the prostate. He was also resuscitated and being prepared for chemoradiation but died before commencement of treatment.

Keywords

Small Cell, Prostate, Cancer, Mortality, Chemoradiation

1. Introduction

Small cell carcinoma of the prostate was first described in 1977 by Wink *et al.* [1]. It is characterized by a locally advanced or metastatic disease with highly aggressive course, rapidly progressive symptomatology, enlarged prostate gland with disproportionate prostate specific antigen (PSA) level (often low level). They also have more predilection for visceral spread and produce lytic bone lesion unlike their adenocarcinoma counterpart [2].

Small cell carcinoma of the prostate is a very rare cancer, constituting less than 1% of all prostate cancers [3], thus, there is paucity of information about its clinical presentation, behavior and optimal treatment options. Small cell carcinoma of the prostate can be a pure or combined disease [4]. Diffuse disease has a survival expectancy of less than 1-year, these tumors are highly aggressive, with a median survival of 9 - 10 months and a 5-year survival of less than 1% [5] [6]; this is similar to the prognosis seen in small cell cancer of the lungs also. Slightly more than half of small cell carcinomas in the prostate are pure without an associated non-small cell component [7]. It has been noted that a large number of cases are detected after androgen ablation therapy for conventional adenocarcinoma of the prostate. In these situations, conventional acinar adenocarcinoma cells may differentiate along neuroendocrine lines [8]. The importance in recognizing small cell neuroendocrine carcinoma is in its histological overlap with primary high Gleason-grade tumors of the prostate and its biological behavior, which will lead to a different clinical presentation and treatment plan [9].

Prostate cancer is the most common incident cancer among men in developed countries, and the 8th leading cause of cancer death globally [10]. Unlike adenocarcinoma of the prostate, small cell carcinoma of the prostate does not express androgen receptors and hence does not respond to androgen ablation, they have a short response to chemotherapy with median survival of 1 year [11] [12].

Here, we discuss two cases of small cell carcinoma of the prostate seen in our facility, their presentation/history, clinical course and the sadly rapid progression of the disease that gave no chance to the patients.

2. Case Reports

The first patient was a 72-year-old retired military officer who presented with a progressively painful scrotal swelling of 3-month duration, and scrotal ulceration and contact bleeding of a month duration associated with a foul-smelling discharge. There was also history of progressive weight lost, loss of appetite and constipation. He however denied any history of lower urinary tract symptoms, dysuria or hematuria, he was not a known hypertensive nor diabetic and was not on

any orthodox medication at presentation, but had several unorthodox and traditional treatment trials with no improvement of his condition. He was pale on examination (packed cell volume of 15%) and lethargic, wasted with a foul smelling exophytic scrotal mass (Figure 1). Serum PSA was 4 ng/l (within normal limit). He was adequately resuscitated. Wedge biopsy and trucut prostate biopsy were done, which revealed small cell cancer of the prostate with scrotal involvement (Figure 2 and Figure 3). Metastatic workup was done and final diagnosis was advanced small cell carcinoma of the prostate. Informed consent was gotten from the patients to take clinical photographs in documentation of the condition and to also take biopsy. Patient was prepared for chemoradiation, had a single dose of chemotherapy but however deteriorated, had multiple organ failure and subsequently died before the second dose.

Figure 1. A huge exophytic scrotal mass with ulcerations and contact bleeding. Notice also, generalized wasting of the patient.

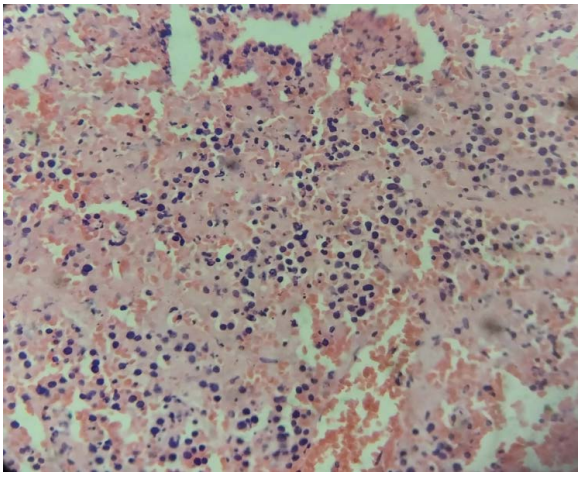

Figure 2. Scrotal biopsy (H&E ×40): Histological sections mainly show tumour necrosis interspersed with some viable small-sized tumour cells with indistinct cytoplasm and hyperchromatic nuclei.

Second patient was a 63-year-old farmer who presented with lower urinary tract symptoms, progressive weight loss and constipation of two months duration, there was also poor appetite and generalized body weakness. The patient is a known hypertensive and diabetic who has also been regular on his medications. He was lethargic on examination, unable to sit or stand without support, pale (PCV of 22%). He was evaluated as a case of benign prostatic hyperplasia to rule out prostate cancer. Result of serum PSA level was 9 ng/L (slightly elevated). Patient had a pelvic ultrasound scan, which shows enlarged prostate gland. He was counselled and informed consent taken for Trucut prostate biopsy, which was done and showed small cell cancer of the prostate **Figure 3**. He was also resuscitated and being prepared for chemoradiation, had pulmonary, visceral (liver) metastasis, deteriorated rapidly and died from cardiopulmonary failure despite adequate resuscitation before commencement of palliative treatment with chemotherapy.

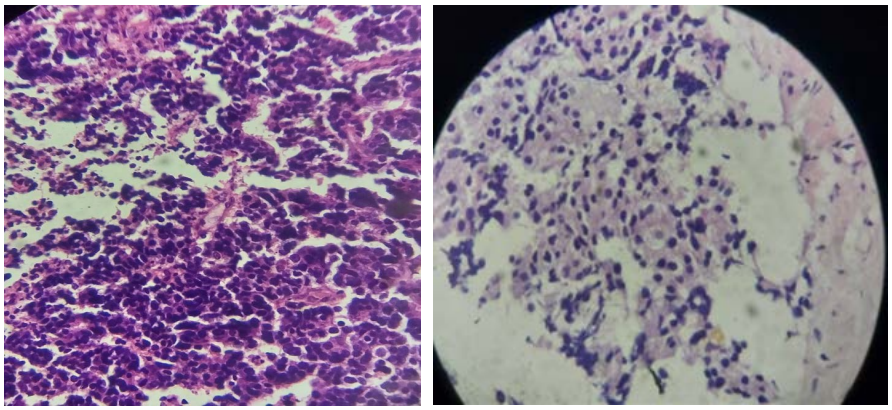

Figure 3. Histological sections of prostate biopsy showing predominantly features of small cell carcinoma (left) admixed with a focus of conventional acinar adenocarcinoma (right).

3. Discussion

Small cell cancer of the prostate is highly aggressive and rare malignancy of the prostate [13], it can occur both as a pure small cell carcinoma or in combination with adenocarcima in which case the level of serum PSA may be elevated, the small cell component being variably distributed in the prostate gland. The prognosis is not affected by the presence of absence of the adenocarcinoma as it is bad in either case with survival less than one and a half years in either case, less than 5% of cases survive beyond 2-year [4] [14] [15]. In our cases, both were lost in less than a year following the appearance of the presenting symptoms.

Unlike adenocarcinoma, small cell carcinoma is hardly incidental, they are mainly symptomatic and present with wide range of symptoms including hematuria, lower urinary track symptoms, paraneoplastic symptoms (Cushing syndrome, hyperparathyroidism, thyrotoxicosis, hypercalcemia) and symptoms of its metastasis to other visceral organs and that of local or contiguous spread/infiltrations [16]. Skin metastasis is largely uncommon [17], for one of our patients, there

was a huge tumor spread and deposit on the scrotal skin producing a foul smelling exophytic and fungating mass. There are reports of local spread to the bladder, pelvic lymph nodes, and distant spread to the lungs, liver, bone, central nervous system and unusual place such as the heart [18]-[20].

Metastatic tendency is very high and metastasis happens early in the disease progression in that at diagnosis more than 75% of the cases already are advanced [21]. Both our two cases were advanced at presentation with both local and distant spread, which is a testimony of this disease's ferocity.

Several theories exist as to the origin of small cell carcinoma of the prostate, one theory postulated that it originated from totipotent stem cells of the prostate which has both epithelial and neuroendocrine types 1, there is also the malignant transformation of normal prostatic neuroendocrine cells rooted in the idea that small cell carcinoma sometimes coexisted with adenocarcinoma hence likely a product of the dedifferentiation of adenocarcinoma based on divergent differentiation model [22], 50% of small cell carcinoma of the prostate is accompanied by adenocarcinoma[23], further buttressing this hypothesis. Another theory linked small cell carcinoma to neural crest line, amine precursor uptake and decarboxylation of prostatic endoderm cells.

Carcinoembryonic antigen (CEA) has been evaluated as a tumor marker for small cell prostate cancer although, it has not been demonstrated as an independent predictor of disease-related outcome [24]. Low Serum albumin level, high serum LDH are important predictors of poor prognosis in small cell cancer of the prostate [25]. Our patients both had low serum albumin level and elevated LDH levels. Other prognostic factors include the state of the disease at presentation, age of the patient, absence of metastasis [26].

Use of hormonal therapy in the treatment of small cell carcinoma of the prostate has been advocated mainly in mixed disease with both small cell component and adenocarcinoma. Hormonal therapy can also be used as an adjunct to radiotherapy [27]. Metastatic disease is mainly treated with chemotherapy. The use of radiation therapy could have a role in the treatment of patients with small cell cancer of the prostate and metastases. Its role is solely for palliation, as it may control local symptoms such as complications of brain and bone metastases [28]. Cyclophosphamide, doxorubicin, vincristine, etoposide, and cisplatin have shown promising outcome in the treatment of small cell carcinoma of the prostate [29] [30]. Surgery is also another treatment modality, radical prostatectomy could be considered when there is no evidence of metastasis (localized disease), Transurethral resection of the prostate may be considered for cases with obstructive voiding symptoms that do not respond to chemotherapy and pharmacologic interventions [28] [31].

Recently, the neuroendocrine cells have become a therapeutic target [32] [33]. This has opened additional options and therapeutic consideration for patients with small cell carcinoma of the prostate. Such agents as somatostatin analogues, neuropeptide-like serotonin and bombesin antagonists, or inflammatory

cytokines, like interleukin-6, are all under investigation in clinical and laboratory settings. However, trials using somatostatin analogues not only for small cell carcinoma of the prostate but also for hormone refractory prostate cancer with or without metastases have attained some success without major adverse effects [34].

Both our patients present with advanced disease and thus surgery was not an option and neither could withstand chemotherapy.

4. Conclusion

Small cell carcinoma of the prostate, though rare, is a vicious and aggressive cancer with varying presentations and high mortality. Disease progression is rapid and prognosis is generally poor. More studies are needed to establish the natural history and best treatment regime for this condition.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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