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Small Cell Prostate Carcinoma: A Case Report, Adenocarcinoma prostrate progressed to small cell prostrate carcinoma and Review of the Literature

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ABSTRACT

Prostatic small-cell carcinoma (PSCC) is a rare tumor that accounts for 0.5–2% of all cases of prostate cancer. It is noteworthy to mention that up to 33% of the cases of PSCC are diagnosed in patients with a previous history of adenocarcinoma of the prostate who may have undergone a treatment in the form of androgen deprivation or radiation therapy. we presented a case 65 year old male T4a N1M1 prostrate adeno carcinoma treated initially with LHRH agonist , abiraterone acetate and zoledronic acid. The first biochemical control after 4 months showed a significant drop of PSA to 0.45 ng/ml. Till August 2019, Patient presented with castration resistant prostate cancer which he received 6 cycle doxetaxel on January 20. In Feb 2020 patient progressed with liver metastasis, pelvic lymph nodes and lobulated mass in rectovessical area. Histopathology of liver biopsy showed small-cell-type neuroendocrine carcinoma. Patient received 6 cycle cisplatin etopside based chemotherapy and showed partial response. In December 20 patient presented with urinary retention while he underwent holium laser enuculation of prostrate under urology department with ureter stent, followed by palliative radiation to prostrate and lumbar bone, however patient still is doing well till date and referred to medical oncology for possible immunotherapy.

INTRODUCTION

Prostatic small-cell carcinoma (PSCC) is a rare tumor that accounts for 0.5–2% of all cases of prostate cancer. The mean age at diagnosis is in the 60s.Prostate cancer is a common malignancy in men, and can be treated successfully if the cancer is of low grade**.** Low-grade tumors are well-differentiated with glandular formation (adenocarcinoma). However, in many patients undergoing androgen depravation treatment, despite of that the cancer becomes castration resistant. One notable tumor type in these advanced diseases is small cell carcinoma. It is highly aggressive, and does not respond well to anti-cancer agents[1] **(*Nadal R et al 2014)*.** PSCC is a very aggressive tumor and has been associated with castrate-resistant metastatic prostate cancer and low prostate specific antigen (PSA) levels, making it challenging to diagnose unless high clinical suspicion or radiologic clue is present. It is noteworthy to mention that up to 33% of the cases of PSCC are diagnosed in patients with a previous history of adenocarcinoma of the prostate.

Pure small cell carcinoma of the prostate (SCCP) is a rare and aggressive disorder that is distinct from the far more common prostatic adenocarcinoma[2],(***Aggarwal R et al 2014)*.**More frequently, prostate cancer (prca) with neuroendocrine (NE) features emerges during disease progression in patients being treated or previously treated with androgen deprivation therapy (ADT) with a prevalence of 0.5–2%.However, SCCP has a prevalence of 10–20% in autopsy reports of men who died of castration-resistant prostate cancer (CRPC)[1]. At diagnosis, most patients are symptomatic because of the extent of the tumor. The aggressive nature and high proliferation rate lead to an increased risk for lytic or blastic bone, visceral, and brain metastases[1].The optimal treatment for patients with metastatic SCCP is not established, but chemotherapy regimens containing a taxane and platinum are often used. Immunotherapy is currently used for platinum-resistant extrapulmonary small cell carcinoma (EPSCC). Up to 60% of patients have tumor reduction with receipt of carboplatin, but the duration of the response is usually short. Despite chemotherapy, SCCP has a poor prognosis, with a median survival of about 10–19 months[3] (***Peverelli G et al 2017)*.**

Case report

In December 2017, A 65 -year-old male, His medical history consisted of hypertensive diabetes mellitus and cardiac right bundle branch block , presented to the emergency department with complaints of dysuria, a decreased urinary stream, and hesitancy for 2–3 month. Physical

examination was mild suprapubic tenderness. associated with fever and chills. He had no symptoms of nausea, vomiting, hematuria, saddle anesthesia, paresthesia, and lower extremity weakness. The finding of the digital rectal examination (DRE) was suspicious of enlaged prostrate, with urine microscropic examination reveals 50-6- pus cell. USG abdomen pelvis shows prostromegaly 35gms with heterogeneous echopattern and significant post void residue. TRUS-guided prostate needle biopsy was taken, and the pathology of the sample was reported as adenocarcinoma with gleasons's score 8(=5+3) grade group 4 involving 70-80% with perineural invasion is present. Magnetic resonance imaging of the pelvis showed prostrate enlarged 4.8x6.8x 4.4cm with extracapsular extention, bilateral seminal vesicles invasion, neurovascular bundle, urinary bladder invasion with pelvic lymphnode shown in fig 1A, B and left acetabulum mixed lytic and sclerotic lesion.

FIG 1A

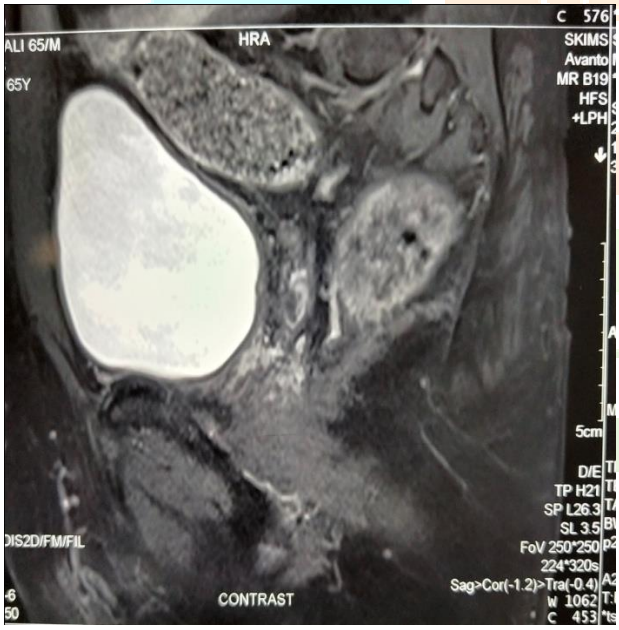
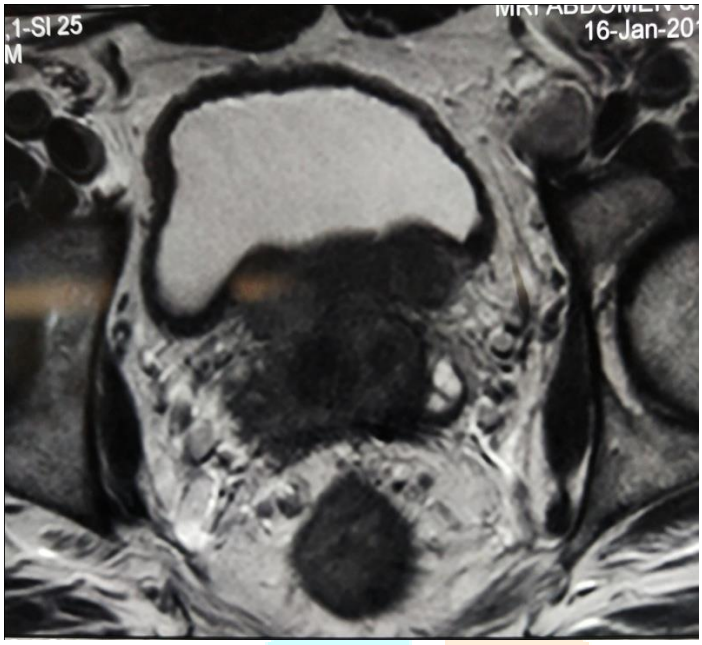


FIG1B



However Computed tomography of the abdomen and chest with contrast was showed a large lobulated prostate suspicious for neoplasm with invasion of the urinary bladder causing bilateral obstructive uropathy. Interestingly, his PSA level reported as 19.76. Patient put on LHRH agonist, abiraterone acetate and zoledronic acid. The first biochemical control after 4 months showed a significant drop of PSA to 0.45 ng/ml. Till August 2019 Patient presented with castration resistant prostate cancer with progressed to lumbar spine metastasis .Patient put on doxetaxel based chemotherapy which he completed 6 cycles on January 20. Computed tomography of the abdomen chest and pelvis with contrast shown liver metastasis, pelvic lymph nodes and lobulated mass in rectovessical area indenting ,infiltrating leftt posterolateral wall of bladder with grade 2 hydronephrosis bilateral,. Histopathology of liver biopsy showed small-cell-type neuroendocrine carcinoma Shown in fig 2.

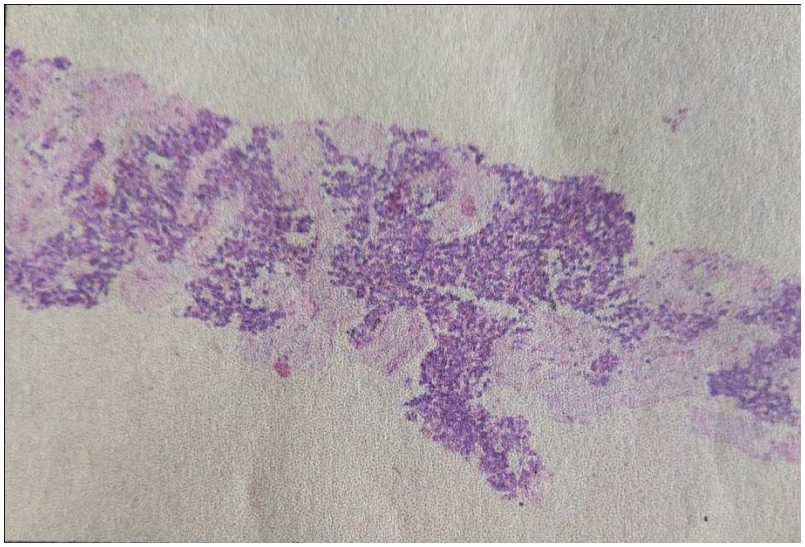


Fig 2

Immunohistochemical staining of the prostate biopsy showed that tumor cells were positive for AE1/AE3, synaptophysin, and chromogranin-A nuroendocrine carcinoma with synaptophysin positive cd56 positive, pan ck positive, ki-67 positive. Patient received 6 cycle cisplatin and etopside based chemotherapy. Post treatment CT scan showed partial response, however no liver mets with localized prostate disease. In December 20 patient presented with urinary retention while he underwent holium laser enuculation of prostrate under urology department with ureter stent, followed by palliative radiation to prostrate and lumbar bone. However patient still is doing well till date and referred to medical oncology for possible immunotherapy.

Discussion

This report presents the first case adenocarcinoma which progress to SCCP. Pure SCCP is a very rare disorder in contrast to the more frequent prca with NE features (also called "aggressive-variant prca"), which emerges during the progression of prca. Whereas the process of neuroendocrine differentiation (NED) after ADT is well known, only few cases of NED after radiotherapy have been described. SCPC is a tumor with a tendency to systemically metastasize and thus has a poor prognosis. Even at the time of diagnosis, nearly 75% of patients are at advanced stage. SCPC has similar features with small cell lung cancer[4] **(*B. Tetu et al1 987)*.**It most commonly metastasizes to the lymph nodes, liver, bone, lungs, pericardium, brain, rectum, and urinary bladder[5]**(*J. H. Rubenstein et al1997)*.**In a 20-case series[4], ***Tetu et al 1987***, reported 2 cases with omental, one case with vocal cord, one case with temporal bone, and one case with adrenal

gland metastasis. SCPC cases have normal levels of PSA and prostatic acid phosphatase (PAP). As the number of cases so far is limited, optimal therapy for SCPC has still to be defined. Extrapulmonary small cell cancers are less sensitive to chemotherapy than pulmonary small cell carcinomas. Chemotherapy and radiotherapy may provide a cure in local disease[6] **(*M. Altınbas et al 2001*).** Survival is less than 1.5years after the diagnosis of SCPC[6].in our case patientt had initially metastatic adenocarcinoma treated with LHRH agonist, , abiraterone acetate and zoledronic acid and doxetaxel based chemotherapy, however Our patient progressed nuroendocrine SCCP almost 2 years after treated as adenocarinoma prostrate with visceral metastasis liver. Histological examination of liver biopsy showed all the features of small cell cancer and patient responded to systemic chemotherapy. We have limited information on the average survival time for the combined prostate adenocarcinoma and nuroendocrine small cell prostate carcinoma because of the limited number of case reports on these cancers in the literature. It is equally unclear which component is more effective for more aggressive behavior and a poorer prognosis of combined prostate adenocarcinoma and small cell carcinoma[7](***S. R. Moore et al 1992***). In one study, patient diagoned as prostrateadenocarcinoma in December 2017 and progress to small cell carcinoma feb 2020 however patient still is doing well till date ,the overall survival time was 9.5 months for combined prostate adenocarcinoma and small cell prostate carcinoma and pure small cell carcinoma, 59.2 months for organ-limited disease, and 8.1 months for widespread disease[8](***T. R. Asmis, et al 2006)***.In another study from MD Anderson cancer center, the average survival time for metastatic small cell prostate cancer was 12.5 months[9](***P. E. Spiess et al 2007***).A study retrospectively assessed data of 30 cases with prostate small cell carcinoma and reported a 4-month disease-free survival with systemic chemotherapy and antiandrogen therapy in a case with pure small cell prostate carcinoma and widespread (metastatic) disease. We also employed antiandrogen hormonal therapy , followed by medical castration as well as radiotherapy to the critical sites of bony lesion , and systemic. The disease became widespread due to rapid progression over a period of 2 year and well respond to EP based chemotherapy and offered immunotherapy .

Conclusion

As small cell prostate cancers are rare, no standard therapeutic regimen exists and the predicted survival is very short. It seems that intense systemic chemotherapy, Typically treated with cisplatin or carboplatin and etoposide-based regimen with or without radiation, antiandrogen therapy, and radiotherapy lengthen the remission period and increase survival time.As small-cell neuroendocrine carcinoma elsewhere in the body, PSC neuroendocrine carcinoma shares many common attributes, including disease rarity, locally invasive disease, advanced stage at the time of diagnosis, prevalence in the 5th or 6th decade of life, aggressiveness, visceral metastasis, and inoperability in some cases., however, it exhibits poor prognosis in most cases among the many other similar features. Nonetheless, management cannot be generalized, and each case should be approached individually.

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