Mikst Primer Prostat Adenokanseri ve Nöroendokrin Diferansiyasyonla Gelişen Prostat Küçük Hücreli Kanseri - Olgu Sunumu

Mixed Primary Prostate Adenocarcinoma and Prostate Small Cell Carcinoma Deriving From Neuroendocrine Differentiation - a case report

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Geliş Tarihi:29.08.2014 Kabul Tarihi: 13.10.2014

Özet

Küçük hücreli prostat kanseri nadir görülen bir kanser tipidir ve tüm prostat kanserleri içerisinde %1'den daha azını oluşturur. Küçük hücreli prostat kanseri klasik adenokanserden klinik ve histolojik olarak farklı özelliklere sahiptir. Blastik kemik metazsazlarına oranla litik kemik metastazı yapma eğiliminde olup labaratuvar olarak da normal yada çok az artmış PSA seviyeleriyle karşımıza çıkmaktadır. Literatürde vaka sayısının az olması nedeniyle ortalama sağkalım süresi hakkında sınırlı bilgi mevcuttur. Hormonoterapiye dirençlidir ve günümüzde küçük hücreli akciğer kanserine benzer tedavi rejimleri ile tedavi edilmektedir. Platin temelli kemoterapi ile başlangıçta iyi bir cevap alınmasına rağmen, tedavi efektif olmamaktadır. Hastalığın prognozu oldukça kötü olup tanı anında ilerlemiş hastalık evresindedir. Ortalama yaşam süresi tanıdan itibaren 2 yıldan kısadır. Burada, prostat adenokanser nedeniyle hormonoterapi alan hastada nöroendokrin differansiasyon ile küçük hücreli prostat kanseri gelişmesi literatür bilgileri eşliğinde bahsedilecektir.

Anahtar Kelimeler: Küçük hücreli, prostat kanseri, nöroendokrin diferansiyasyon

Abstract

Prostate small cell carcinoma is a rare malignancy and accounts for less than %1 of all prostatic carcinomas. It separates with lots of clinical and histological features from classic adenocarcinoma. Contrary to adenocarcinoma , small cell carcinoma is found to have lytic bone metastasis and serum PSA level is within normal range or increased only a little quantity. Due to limited number of case reports in literature, there is a little information about median survival time. It is hormone-resistant and treatment regimen is found to be similar to small cell lung cancer. In spite of good response at initial, platinum-based chemotherapy is not an effective treatment. Prognosis is rather poor and most of the patients have advanced stage at the time of the diagnosis. Median survival time is less than 2 years from following initial diagnosis. Herein, we reported small cell carcinoma derived from neuroendocrine differentiation in a patient who was priorly treated with hormone therapy for prostate adenocarcinoma, in the light of the literature.

Keywords: Small cell, prostate cancer, neuroendocrine differantiation,

Introduction

Prostate cancer is the most common malignancy in men and it is an important source of mortality and morbidity. [1] Histological type is generally adenocarcinoma which derives from transformation of prostate glandular cells. Prostate small cell carcinoma is a rare malignancy presenting with advanced disease at the time of diagnosis and has an estimated incidence of %1 in all prostate cancers. Mean presentation age is 65 year[2] and about 50% of patients have pure small cell carcinomas at initial presentation. About 25%-50% cases are mixed with conventional adenocarcinoma of prostate. Another 25% to 40% are initially diagnosed as adenocarcinoma and represent as small cell carcinoma after hormone therapy. [3] In contrary to adenocarcinoma, this rare type does not secrete prostate specific antigen and presents with mostly lytic bone lesions.[4] Treatment response between small cell prostate cancer and small cell lung cancer is found to be similar. Platinum-based chemotherapy (especially cisplatin and etoposide combination) is mostly used. Radiotherapy is used to control local disease or as a palliative option for extensive disease. It has a poor prognosis with a median survival time ranging from 6 to 17 months from following initial diagnosis.[5] Small cell carcinoma derived from neuroendocrine differentiation is supposed to be secondary to androgen blockade treatment which is mostly used and successful in classical adenocarcinoma.

Case

A 56-year-old male patient with medical past history of chronic obstructive lung disease and coronary artery disease presented to hospital urology department with 3 months duration of pelvic pain and lower urinary tract symptoms including difficulty in urination and dribbling of urine. On physical examination patient had no significant finding. Digital rectal examination revealed a larger prostatic gland and hard prostatic nodul in the center area of the gland. Urinary ultrasonography showed an enlarged prostate size of 43x51x46 mm. Total PSA was at a higher level of 85 ng/mL and other labaratuary findings were unremarkable. Patient underwent intervention of transrectal ultrasound guided biopsy. Pathological findings showed gleason score 7 (4+3) prostatic adenocarcinoma along with poorly differentiated neuroendocrine cancer stained positive for CD56, chromogranin, synaptophysin and TTF-1 (figure-1,2). Abdominal computer tomography screening and whole body bone scintigraphy identified blastic bone metastasis at inferior part of scapula and posterolateral part of L4-L5 vertebrae. Patient was commenced on hormone therapy of bicalutamide plus leuprolide for maximal androgen blockade. One months after initiation of hormone therapy, patient's PSA level was within normal range. Six months later patient represented complaining with lumbar pain and voiding difficulty. Serum creatinine level was 6,5 mg/dL that had increased from the baseline 0,8 mg/dL. An urinary ultrasonography revealed bilateral urinary grade 2 hydronephrosis. Pelvis magnetic resonance screening showed enlarged prostate with a big mass arising from prostatic gland size of 67x67x105 mm (figure-3). Whole body bone scintigraphy detected lytic metastasis at 11th costa of right hemithorax. Serum creatinine levels gradually decreased after bilateral urinary nephrostomy catheter was performed for releasing the urine stream. PSA levels were within normal range. A new prostate biopsy was full of tumoral formation and characterised with wide layers of inflamed tumor stroma, formed trabecular or in groups, small-to-medium-sized, hyperchromatic nuclei and narrowed cytoplasm of which boundaries were ineligibility. These findings were interpreted as small cell carcinoma of the prostate which was positive for synaptophysin and chromogranin and negative for PSA (figure-4,5). Patient was discussed at multidisciplinary team meeting and case was accepted as adenocarcinoma along with small cell carcinoma arising from neuroendocrine differentiation. Chemotherapy combination of cisplatin plus etoposide was planned once a 3 week. On follow up patient developed massive pulmonary embolism and died of cardiopulmonary arrest.

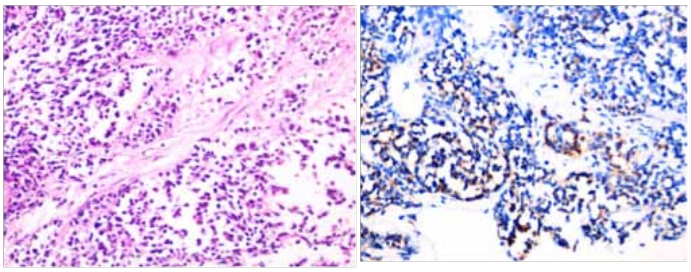


Figure 1 and 2 : Prostate adenocarcinoma with neuroendocrine differentiation



Figüre-3: Magnetic resonance screening of pelvis

A large mass which completely fills prostatic gland and invades the bladder and causes local wall thickness.

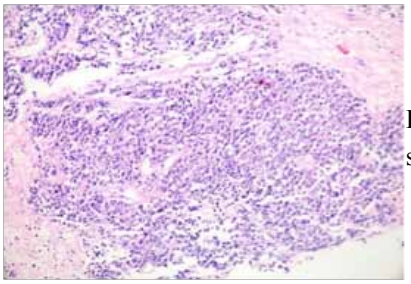


Figure-4 ; Prostate small cell cancer

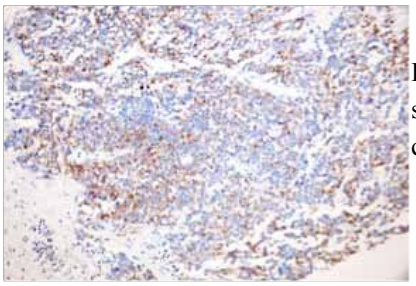


Figure-5; positive staining for chromogranin

Discussion

As aforementioned in this article, about 50% of patients have pure small cell carcinomas at initial presentation. About 25%-50% cases are mixed with conventional adenocarcinoma of prostate. Another 25% to 40% are initially diagnosed as adenocarcinoma and represent as small cell carcinoma after hormone therapy. In this case patient represented as small cell carcinoma derived from neuroendocrine differentiation 6 months after initiation of hormone therapy for classical adenocarcinoma.

Neuroendocrine cells are found from %10 to %100 in all prostate cancer cases depending on used technique. [6,7] Neuroendocrine differentiation in prostate cancers can occur using one of three following form ; small cell carcinoma, carcinoid-like tumors and neuroendocrine differentiation in a conventional adenocarcinoma.[8,9] In our case neuroendocrine manifestasion was consistent with the last form. Although initial diagnose was metastatic prostate adenocarcinoma, subsequently small cell carcinoma developed from neuroendocrine differentiation due to neuroendocrine cells lack of androgen receptors. Most likely, this manifestation is supposed to occur with neuroendocrine cell proliferation secondary to androgen blockade treatment.

Small cell prostate carcinoma can be easily differentiated from conventional prostatic adenocarcinoma with lytic bone tropism, normal range of PSA and PAP, negative staining for androgen receptors and positive staining for chromogranin and synaptophysin in biopsy specimens. Abrahamson reported that increased levels of neuroendocrine products are related with poor prognosis. [10] In our case, patient recurred with small cell cancer with normal PSA levels and positive staining for synaptophysin and chromogranin. Bone metastasis were in lytic character more than blastic. Laboratory findings were consistent with the datas reported by Petraki et al who showed 86% positive staining for synaptophysin, 71% positive staining for chromogranin.[11] CD56 and TTF-1 are also helpful markers in distinction of small cell carcinoma from adenocarcinoma. Our patient's biopsy was positive for these two markers.[12]

Small cell prostate carcinoma has some similar characteristics with small cell lung cancer.[13] Patients may present with inappropriate ADH secretion[14] or ectopic ACTH syndrome.[15] Treatment approach and response rate are found to be similar with small cell lung cancer. There is not yet a standard chemotherapy regimen, however platinum-based chemotherapy is mostly used. Despite positive initial response, this chemotherapy regimen modality fails to be effective standard treatment. Studies suggest that oral estramustine along with etoposide treatment has good response rates comparing with addition of doxorubicin to cisplatin and etoposide.[16,17] Extrapulmonary small cell cancer is less sensitive to chemotherapy unlikely small cell lung cancer. Chemotherapy and radiotherapy may control local disease.[18] Average survival time is less than 1,5 year from following initial diagnosis.[13] In our case, patient died 2 weeks after first cycle chemotherapy due to cardio-pulmonary arrest secondary to pulmonary embolism.

Conclusion

Prostate small cell cancer is a rare and aggressive prostatic malignancy. Despite the fact that treatment modality is similar to those small cell lung cancer, prognosis is poor and chemotherapy and radiotherapy seems to be as a palliative options. In this case, patient's initial diagnosis was adenocarcinoma but in representation subsequent biopsy revealed small cell carcinoma which was supposed to occur from neuroendocrine component after hormone therapy.

So, if patient with prostate adenocarcinoma represents as disease progression while PSA levels are normal, neuroendocrine differentiation should be kept in mind and re-evaluation should be performed as soon as possible.

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