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Abstract

Introduction. Prostate cancer is one of the most common malignancy in men. The most common type is acinar adenocarcinoma. Small cell prostate cancers (SCPC) usually occur together with coexisting prostate adenocarcinoma. Case report. A 72-years-old patient with voiding symptoms. Initial prostate specific antigen (PSA) is 2.87 ng/ml. Twelve prostate biopsies were taken and in six of them neoplastic tissue was detected. Viewed tissue is most convenient to “small cell carcinoma”\(^{1}\). Bone scintigraphy has not established dissemination of cancer in skeletal system. MSCT of pelvis has not found any special pathology changes. The patient underwent surgery - radical retropublical prostatectomy. Histopathological analysis revealed a poor differentiated adenocarcinoma of the prostate with small cell carcinoma zones. Gleason score 5+5 (10), grade III, pT3bN1, stage IV.

Conclusion. Poorly differentiated adenocarcinoma prostate, especially in combination with small cell prostate cancer, is an aggressive malignancy with most cases presenting with extensive disease dissemination on diagnosis and poor prognosis. Small cell carcinomas of prostate are extremely rare tumors of the neuroendocrine origin. Patients with mixed prostate cancer, compared to pure small cell prostate cancer, have a better prognosis and greater survival rate. There is a lack of evidence guiding treatment for SCPC.

Key words: prostate, cancer, small cell, prostate specific antigen.

Apstrakt


Ključne reči: prostate, karcinom malih ćelija, prostata specifični antigen.
Introduction

Prostate cancer is one of the most common malignancy in men. In the United States of America it is on the second place, immediately after lung cancer. It is also the leading cause of mortality in males. The most common type is acinar adenocarcinoma. Small cell prostate cancers (SCPC) usually occur together with coexisting prostate adenocarcinoma. Carcinoma of the prostate can be divided into two groups: acinar and non-acinar. According to certain data, non-acinar prostate tumors can be found in 5-10% of patients with prostate malignity. Small cell prostate cancer is one of the rarest type of prostate cancer and makes 0.3–1% of all prostatic tumours. It is not known incidence of prostate adenocarcinoma with a small cell component in Serbia and also in Southeast Europe. In the available literature are not found reported cases of this type of prostate cancer in Southeast Europe.

Case report

A 72-years-old patient with voiding symptoms which started six months before his first visit to urology specialist. A patient suffering from arterial hypertension, which is controlled by medication. First was conducted diagnostics which included digitorectal examination, the value of PSA in the blood and transrectal ultrasound of prostate. Inicial prostate specific antigen (PSA) is 2.87 ng/ml. Other laboratory findings (urinalysis, white blood cells, erythocyte sedimentation rate) were unremarkable. A transrectal prostate biopsy with pathohistology examination was indicated, because during digitorectal examination at the left lobe of prostate was found one nodule of stiffer consistency. Twelve prostate biopsies were taken and in six of them neoplastice tissue was detected. Tumor tissue is built of round atypical cells with hiperhromic vesicular nuclei, focally visible nucleus and sparingly cytoplasm. Tumor cells lesser extent grade short sequences and less solid beach and a large part in the non cohesive schedule. Viewed tissue is most convenient to “small cell carcinoma”. In immunohistochemistry analysis of prostate samples the following immunofenotypes were discovered: TTF-1+, Ckae 1/ae3+, Ki-67~65%, CD117+, CD56-, Chromogranin A-, Synaptophysin -, NSE-, CK7-, CK20-, BCL2-, LCA-, CD99-. These finding are substantially compatible with prostatic „small cell“ carcinoma. Inicial prostate specific angigen (PSA) is 2.87 ng/ml. Bone scintigraphy has not established dissemination of cancer in skeletal system. MSCT of pelvis has not found any special patology changes in anatohmy – prostate dimension is 40x54 mm, there are parenhimal calcifications and capsula of prostate is clearly limited. Also, there was not present any sign of retroperitoneal lymphadenomegaly. The patient underwent surgery - radical retropubical prostatectomy. Histopathological analysis of surgically removed tissues and organs revealed that it was a poor differentiated adenocarcinoma of the prostate with small cell carcinoma zones in poorly differentiated areas. Tumor invades both lobes of the prostate and prostatic capsule penetrating to the infiltration of both seminal vesicles. Operational been removed twenty-two lymph nodes and in two of them metastases are present. There were also present PIN low and high grade. Gleason score 5+5 (10), grade III, pT3bN1, stage IV. Prostate size was 5x4.5x3.5 cm. (Figure 1).
By oncologist indication, the patient postoperatively received four cycles of chemotherapy, according to the protocol etoposidium and cisplatin, at the Oncology Institute of Vojvodina. Patient also has started therapy with luteinizing hormone-releasing hormone (LHRH) antagonists. The PSA value during hormone therapy is 0.7 ng/ml.

The patient's general condition is gradually worsening one year after the chemotherapy has been performed. A complete body skeleton scintigraphy in the anteroposterior and posteroanterior projection with a 99mTc-DPD was performed showing a diffusely pronounced pathological hyperfixation of the radiolabel in the axial and appendicular part of the skeleton. This finding suggests the diffusion of the basic pathological process into the bone joint system (Figure 2).

**Discussion**

The most frequent presentation in humans of neuroendocrine tumors are in prostate gland, lungs, and pancreas 8. One third of patients with SCPC already suffered from prostate adenocarcinoma. The average age of these patients are between fifty and seventy years of age 9. Metastasis appears in 60% of cases with rate between five to eighteen months. All patients observed with mixed prostate cancer had better survival rate 8. Clinical presentation of SCPC and adenocarcinoma is quite different, obstructive uropathy as well as dissemination of disease dominate with patients suffering from SCPC 9. Aggressive clinical course took place in most of the cases with small cell adenocarcinoma 10. Most of the patients, when diagnosed, already had advanced stage of disease 9. Lungs were most frequently included. Bladder, liver, and bone were also targeted. Almost all of the patients had symptoms typically related to enlarged prostate gland. Low grade fevers also appeared with some of the patients which are attributed to underlying malignancy. In patients with SCPC PSA level may not be elevated, or having PSA level not in proportion with tumor size. Neuroendocrine markers, including chromogranin, CD 56, synatophysin, and neuron specific enolase are usually positive when SCPC is diagnosed 11,12. In at least 90% of the cases with SCPC these markers were positive. It is well known that serum PSA never correlate with burden of disease, although prostatic adenocarcinoma and SCPC can occur concomitantly 13. PSA levels could be elevated in patients with mixed prostatic adenocarcinoma and SCPC. Since that condition occurs very seldom, there could be the lack of evidence guiding treatment for SCPC 11-14. There are few possibilities of treatment such as surgery, chemotherapy, and radiotherapy. The course of therapy is mainly defined depending on the stage of disease 13. Prospective randomize trials were precluded due to rarity of the disease. The therapy is mainly modeled after those in small cell carcinoma of lungs. Chemotherapy is mainly used (cisplatin and etoposide) as main treatment, cause the aggressiveness of the disease. Response to treatment is the most important thing when we estimate the survival. Increased survival rated is noted in patients that underwent radical surgical resection in combination with other treatment modalities had an important role in better survival rate. Metastatic symptoms as well as local disease control can be treated with radiotherapy 14. Hormonal therapy is not recommended in pure SCPC, and is still controversial in mixed histologies. Neuroendocrine differentiation development could be associated with it in other forms of prostate cancer. Poor prognosis is notified in patients having Gleasone score 8 or greater after radical prostatectomy, especially if nodal metastasis are present as a most important prognostic factor 12,15.
Poorly differentiated prostate adenocarcinoma, especially in combination with small cell prostate cancer, is an aggressive malignancy with most cases presenting with extensive disease dissemination on diagnosis and poor prognosis. Early detection has a role in improving prognosis, is, however, rather challenging. Further research is required to establish a standard treatment protocol, in order to reduce the mortality rate and extend patient survival.

REFERENCES


Fig. 1 – Operational removed prostate gland with macroscopically visible tumor.
Fig. 2 – A complete body skeleton scintigraphy in the AP and PA projection with a 99mTc-DPD, one year after the ending of chemotherapy.

SUBSCRIPT

SCPC - small cell prostate cancers
PSA - prostate specific antigen
LHRH - luteinizing hormone-releasing hormone

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