Mucinous adenocarcinoma of the Prostate –a case report

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Abstract

Mucinous aenocarcinoma is one of the least common variant of prostate cancer. The prognosis of this variant of prostate cancer remains controversial. We report the case of 67-year old men with severe lower urinary tract symptoms (LUTS), bladder outlet obstruction (BOO), and sense of urinary retention. The serum level of prostate specific antigen (PSA) was 10.4ng/mL. Prostate was large (56mL), hard, lobulated, with extraprostatic extension and infiltration of surrounding structures, unsuitable for radical operative treatment. The patient demonstrated poor response to complete androgen blockade (CAB) (bilateral orchiectomy, steroidal antiandrogen) after 6 months of treatment with minimal decline of PSA (7.1ng/mL) and progressive growth of the primary tumor (110mL). The patient is submitted to antiandrogen withdrawal consisted of simultaneous addition of ketoconazole with hydrocortison substitution, resulting in normalisation of PSA (<1.0ng/mL) and diminution of prostate volume (PV) (63 mL) after 2 months, followed by adjunctive radiotherapy. Ketoconazole in reduced doses was stopped 6 months after completion of radiotherapy with PSA level < 0.002ng/mL and PV 16mL. The patient is alive with no evidence of disease more than 9 years after diagnosis of primary tumor. This case demonstrated modest hormonal sensitivity of mucinous adenocarcinoma of the prostate, whereas ketoconazole combined with radiotherapy, resulted in long term survival.

Ključne reči: prostate cancer, mucinous adenocarcinoma, complete androgen blockade, bilateral orchiectomy, steroidal antiandrogen, ketoconazole, irradiation.

Mucinozni adenokarcinom prostate – prikaz slučaja

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Apstrakt

Mucinozni adenokarcinom je jedan od najredjih varijanti karcinoma prostate. Prognoza ove vrste karcinoma prostate je kontraverzna. Iznosimo slučaj 67- godina starog muškarca sa jako izraženim simptomima donjih partija urotrakta, opstrukcije na nivou vrata mokraćne bešike i osećaja retencije urina. Nivo prostata specifičnog antigena (PSA) u serumu je bio 10.4ng/mL. Prostata je bila uvećana (56mL), tvrda, lobulirana, sa ekstraprostatičnim širenjem i infiltracijom okolnih struktura, nepodobna za radikalno operativno lečenje. Pacijent je pokazao slab odgovor na kompletnu androgenu blokadu (bilateralna orhiektomija, steroidni antiandrogen) posle 6 meseci tretmana, sa minimalnim smanjenjem nivoa PSA (7.1ng/mL) i progresivnim uvećanjem primarnog tumora (110 mL). Obustavljeno je davanje antiandrogena, uz simultani dodatak ketokonazola i substituciju hidrokortizonom, što je rezultiralo nomalizacijom PSA (< 1.0 ng/mL) i smanjenjem volumena prostate (63 mL) posle 2 meseca, čemu je sledila dodatna radioterapija. Ketokonazol u smanjenoj dozi je obustavljen 6 meseci posle završetka radioterapije sa vrednostima PSA < 0.002 ng/mL i smanjenjem volumena prostate na 16 mL. Pacent je živ i bez znakova bolesti više od 9 godina od postavljanja dijgnoze primarnog tumora. Ovaj slučaj pokazuje skroman efekat konvencionalne hormonalne terapije kod mucinoznog adenokarcinoma prostate, dok je ketokonazol u kombinaciji sa radioterapijom, rezultirao preživljavanjem za duži vremenski period.

Key words: karcinom prostate, mucinozni adenokarcinom, kompletna androgena blokada, bilateralna orhiektomija, steroidni antiandrogen, ketokonazol, iradijacija.

Introduction

Mucinous adenocarcinoma of the prostateis a rare morphological variant, with incidence of approximately 0.2-0.4%, characterized by large pools of extracelular mucin present in at least 25% of tumor volume[1,2]. Grading and prognosis of these rare type of prostatic cancer remain debatable[3-5]. There is no concensus on how mucinous prostatic carcinoma should be scored [6]. Some authors suggest that a gleason score of 8 is to be assigned, whereas others recommend ignoring mucin and grading tumor based on the underlying architectural pattern 7. Patient with mucinous prostatic adenocarcinoma have increased PSA with advanced disease and occasionally followed with widespread metastasis[1,4,8,9], while others authors reported excellent outcome with radical prostatectomy[5,10].

We report the clinical course of a locally advanced mucinous prostatic adenocarcinoma and increased PSA level, managed initially with poor response with CAB (bilateral orchiectomy and steroidal antiandrogen), followed by salvage treatment with ketoconazole and radiotherapy.

Case report

At the end of January 2006, a 67-year old men presented with severe LUTS (International Prostate Symptome Score [IPSS] 26, Quality of Life Score [QOLS] 6), BOO (peak flow rate [PFR] 6.0 mL/s, mean flow rate [MFR] 8.0 mL/s, postvoiding residual [PVR] 230 mL) and elevated PSA value of 10.4 ng/mL. Otherwise, patient's father died at 52- years of age due to metastatic prostate cancer. Clinical examination demonstrated the presence of enlarged (56 mL), hard and nodular prostate, with extraprostatic extension and infiltration of both vesicles and rectum. Histology at prostatic biopsy revealed the presence of mucinous adenocarcinoma of the prostate. CT scan and bone scintigraphy confirmed the absence of metastasis. The case was qualified as not suitable for radical operative treatment. Patient is submitted to CAB : bilateral orchiectomy with antiandrogen (cyproterone acetate, 200 mg daily). After 3 months PSA dropped to 2.0 ng/mL, IPSS was 1, QOLS 1, PFR 16 ml/s, MFR 11.0 mL/s, and PVR 110 mL. However, local progression of the primary tumor was noted, with PVmeasuring 65 mL. Three months latter PSA passed to 7.1 ng/mL, with extensive local growth of the tumor (PV 110 mL), but without any subjective and objective signe suggestive for LUTS. Antiandrogen withdrawal during 2 months consisted of simultaneous addition of ketoconazole (inetrmediate doses, 900 mg daily) with hyrocortisone substitution (30 mg daily), which resulted in decline of PSA (< 0.1 ng/mL) and decrease of PV (63 mL).The treatment was followed with adjunctive 3D conformal radiotherapy (total dose of 65 Gy, 33 fractions). Patient continue the treatment with reduced doses of ketoconazole (600 mg daily) during 6 months, while hydrocortisone was discontinued previously due to fluid retention symptoms, with consistently PSA value < 0.002 ng/mL, and diminution of PV progressively to 16 mL. Ketoconazole was stopped on November 2007, and patient is disease free, maintaing a healthy, active lifistyle, more than 7 years after completion of treatment. The patient is followed once yearly with PSA, digital rectal examination and transabdominal ultrasound examination. We plan to restart treatment at PSA value > 2.0 ng/mL.

Discussion

Despite that intraluminal mucin is seen in almost 33% of prostate cancer, diagnosis of mucinous adenocarcinoma can be made only when the amount of extracelular mucin is sufficiently large as to produce pools of mucus. Therefore, it is better to use a term „prostatic adenocarcinoma with focal mucinous areas"[7]. Acording to the literature, only a small proportion of mucinous tumors are accompained by positive signet cells in the mucin11. There is a discrepance regarding outcome in terms of hormone sensitivity and recurence[2,8,9,12]. Mucinous adenocarcinoma of the prostate behave agressively[1,4,13], but other authors found that reversal experience[2,5,4].

Osunkoya et al. demonstrated an excellent prognosis of mucinous adenocarcinoma of the prostate in a series of 47 casese managed by radical prostatectomy, with 5-year progression –free survival of 97%, in comparison of 85% for nonmucinous prostate cancer. These authors founded that mean mucinous component in the tumor was 52%, the mean preoperative PSA level 9.0 ng/mL, with mean Gleason score 6 (13%) and 7 (79%)[10]. Lane et al. compared 14 patients with mucinous adenocarcinoma of the prostate with 18 other patients who had prostate cancer with focal mucinous features and reported that the former behaved clinically in a very similar fashion to the latter[5].

Saita and Iwaki reviewed 87 cases of mucin-producing prostatic carcinoma, and found that prognosis is worse in those with signet-ring cells[4]. Mucinous adenocarcinoma of the prostate with signet-ring cells had a very poor prognosis in contrast to signet-ring cell carcinomas alone. Johnson et al. showed that ERG gene expression in mucinous adenocarcinoma of the prostate and prostatic adenocarcinoma with mucinous features is similar to rates of expression in acinar prostatic adenocarcinoma. This study strongly suggests that these rare subtypes of prostatic carcinoma are clonally related to conventional prostatic cancer[7].

It is probable that the low metastatic potential of prostatic cancer in our case was a result of the low/intermediate Gleason score and not of the presence of mucin pool. The limitation of our histological finding is related with the absence of Gleason score determination in bioopsyspecimen. Although these tumors are not as hormonally responsive as their nonmucinous counterparts, some tumors respond to androgen withdrawal. We used antiandrogen withdrawal accompained by simultaneous administration of ketoconazole, which resulted in prompt normalisation of PSA level (< 1.0 ng/mL), diminution of PV, followed by adjunctive radiotherapy. Small et al. reported that simultaneous addition of ketoconzole to antiandrogen withdrawal, produced a significant increased PSA response (32% vs. 11%) and longer time to PSA progression (8.6 vs. 5.9 months) compared to antiandrogen withdrawal[14]. The present study confirmed excellent response to ketoconazole, after failure to initial CAB, combined with radiotherapy, since the patient was not motivated for radical prostatectomy, particularly having in view his excellent urinary status.

Conclusion

We report a case of localized infiltrative mucinous adenocarcinoma of the prostate with excellent outcome and long-term survival after combined therapeutical approach (CAB, ketoconazole, radiotherapy). Mucinous adenocarcinoma appears to behave clinically in a similar fashion to conventional adenocarcinoma of the prostate, and does not confer poor prognosis.

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