

Case report

## Prostate cancer in an elderly patient with a history of comorbidities

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### ABSTRACT

Prostate cancer is the most common cancer in men in Poland. The choice of treatment method depends on many factors, including the stage of the disease, the patient's age, life expectancy, the presence of comorbidities and the general condition of the patient. Hormone therapy is one of the basic methods of prostate cancer treatment, both in adjuvant and palliative treatment. Castration-resistant prostate cancer is an incurable disease. However, the introduction of new hormonal drugs to therapy significantly extended the survival time of patients with relatively low harmfulness of therapy.

**Key words:** prostate cancer, hormone therapy, nmCRPC, apalutamide

## INTRODUCTION

Prostate cancer is the most prevalent cancer in men in Poland. It is characterised with the greatest dynamics of morbidity growth with simultaneous mortality increase. It is the third cause of death in the cancer mortality ranking in the male population [1].

Radical prostatectomy, radiotherapy, and pharmacological castration are among fundamental prostate cancer treatment methods [2]. The initial non-response to androgen deprivation therapy (ADT) in prostate cancer is an important biological turning point in disease progression, which signals a related higher risk of death. The non-response is caused by selective proliferation of cancer cells insensitive to androgens that were originally present in the environment in a low number or appeared as a result of gene mutation, resulting in total population of cancer cells becoming largely insensitive to hormones. The loss of ADT efficacy in inhibiting the disease activity results in greater tumour growth and higher PSA (prostate-specific antigen) blood levels, which leads to the development of castration-resistant prostate cancer (CRPC) [3].

According to the definition by EAU (European Association of Urology), CRPC occurs when, despite achieving castrate blood testosterone level ( $< 50$  ng/dL or  $< 1.7$  nmol/L), disease progression is:

- biochemical – three consecutive increases of PSA levels at the interval of at least one week resulting in two increases by 50% vs. nadir level at nominal PSA level  $> 2$  ng/mL
- radiological – occurrence of two or more osteolytic lesions in bone scintigraphy scan or lesions in soft tissues according to RECIST (Response Evaluation Criteria in Solid Tumours) [4].

In most patients, metastases develop before achieving the CRPC condition. In some patients, however, conventional imaging scans (scintigraphy, CT) do not reveal any metastases. Such patients are referred to as nmCRPC (non-metastatic CRPC), while 30% of them will develop remote metastases during the next 2 years [5].

In the treatment of nmCRPC with a high risk of disease progression, one should consider administration of apalutamide, darolutamide, or enzalutamide [6]. Apalutamide and enzalutamide are more effective in the treatment of nmCRPC, whereas darolutamide is characterised with higher tolerance. Considering the comparison of overall metastasis-free survival achieved during the treatment with the above drugs, apalutamide seems to be the best treatment option [7]. In the SPARTAN study, the metastasis-free survival median in the group treated with apalutamide

in combination with ADT was by 24.3 months longer than in the group administered placebo plus ADT. Time until metastases and disease progression free survival rate were also statistically significantly better than the results obtained in the control group [8].

## CASE STUDY

On 15 September 2008, a male patient aged 72 at the time reported to urological emergency due to urinary retention after a family event with abundant amounts of alcohol. The patient had no chronic diseases. He was diagnosed with urinary retention with concomitant urinary infection. In additional tests: CRP = 31 mg/mL, PSA = 40 ng/mL, in urine – leukocytes covering the visual field. The patient was catheterised and treated with a broad-spectrum antibiotic. During consecutive visits at the urological outpatients', a drop in CRP was observed, with alleviation of urinary inflammation symptoms, as well as PSA level reduction to 14.5 ng/mL. After 4 weeks, the catheter was removed. Due to lesions observed in prostate USG, suspected to be neoplastic proliferation, on 4 March 2009, the patient was qualified for core biopsy of the prostate. Histopathological test result: adenocarcinoma prostatae Gleason 5 (2+3) at PSA = 15.2 ng/mL.

The patient was qualified for radical prostatectomy on 22 April 2009. Histopathological test result: adenocarcinoma Gleason 5 (2+3), no infiltration of blood vessels or nerves observed, positive margin on the side of right seminal vesicles; pT3aN0M0 R1.

The patient was qualified for radiotherapy: supplementary therapy focused on prostate area with the dose of 66 Gy/33 fractions in the period 15 Sept.–28 Oct. 2009. The patient was under control of urological outpatients'.

In 2015, the patient was diagnosed with rectal cancer. On 12 May 2015, the patient was qualified for anterior rectal cancer resection. Histopathological test result: adenocarcinoma G1; pT2N0M0. The patient did not require supplemental treatment. He was transferred for further observation at the oncological outpatients'. In the meantime, the patient was diagnosed with hypertension, type 2 B diabetes, chronic kidney disease stage 2, as well as degenerative spine condition.

Starting from May 2017, gradual PSA progression was observed. Computed tomography (CT) scan of the chest and true pelvis, magnetic resonance imaging (MRI) of the true pelvis, and bone scintigraphy did not reveal any symptoms of metastases. PET-CT scan using  $^{68}\text{Ga}$  revealed local recurrence hence, in October 2017, at PSA level of 2.1 ng/mL, the patient was qualified for

hormonotherapy. Treatment with flutamide was instituted at the dose of 750 mg/24 h for one month. After 3 weeks of the treatment, it was supplemented with the treatment with LHRH (luteinizing-hormone-releasing hormone) analogue – leuprorelin acetate administered every 6 months. After the treatment, PSA was reduced to 0.036 ng/mL (nadir: February 2018).

Starting from March 2021, slow increase in PSA was observed, with dynamic growth from September 2021: 0.25 ng/mL (27 Sept. 2021), 1.4 ng/mL (15 Nov. 2021), 2.1 ng/L (10 Jan. 2022). The patient performed the planned imaging scans: CT of the thoracic and abdominal cavities and true pelvis, MRI of true pelvis, and bone scintigraphy. The scans did not reveal cancer recurrence or metastases.

On 14 Feb. 2022, the patient was qualified for treatment under the drug programme established by the Polish National Health Fund based on apalutamide at PSA value of 2.9 ng/mL. Despite the advanced age (86) and comorbidities upon the onset of apalutamide treatment, the patient was autonomous in all everyday life areas, lived by himself, with his WHO functional ability scoring 0.

During the treatment, a control bone scintigraphy was performed on 11 Aug. 2022, as well as CT of the thoracic and abdominal cavities and true pelvis on 4 Aug. 2022. No symptoms of

metastases were observed. The next checkpoint falls in February 2023. During the control tests on 9 Nov. 2022, PSA decrease was observed to the level of 0.022 ng/mL. No side effects of the treatment were recorded.

## DISCUSSION

The inclusion of three new generation androgen inhibitors: apalutamide, enzalutamide, and darolutamide, together with ADT (androgen deprivation therapy) in the treatment of nmCRPC patients with high risk of metastases created an option of extending overall survival and metastasis-free survival in the group. The treatment involves maintenance of patients' good quality of life because nmCRPC is usually asymptomatic. The administration of new generation inhibitors in nmCRPC patients with high risk of metastases also has a psychological aspect (alleviated fear resulting from PSA progression).

One must remember that CRPC is incurable, but usually of long duration, often lasting many years. The introduction in the drug programme established by the Polish National Health Fund of three new generation inhibitors for nm-CRPC patients with high risk of metastases is a good option for extending survival in this group of patients while simultaneously offering them a good quality of life.

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