American Journal of Medicine and Medical Sciences 2023, 13(2): 60-62
DOI: 10.5923/j.ajmms.20231302.06

Peculiarities of Clinical Course and Diagnostics of Castration-Resistant Prostate Cancer

Tillyashaykhov Mirzagolib Nigmatovich[1], Iskandarov Jakhongir Mashrabjon Ugli[2], Boltaev Mashrab Iskandarovich[2], Boyko Elena Vladimirovna[3], Nodir Makhamatkulovich Rahimov[4]

[1]Doctor of Medical Sciences, Professor Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology, Uzbekistan
[2]Bukhara Branch of the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology, Uzbekistan
[3]Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology, Uzbekistan
[4]Doctor of Medical Sciences, Samarkand State Medical University, Uzbekistan

Abstract The aim of this article was to study the peculiarities of clinical course and diagnostics of primary castration-resistant prostate cancer. The study was based on the data analysis of 112 patients with hormone-resistant prostate cancer (HRPC) under observation at the oncourology department of the RSNPMCRC from 2008 till 2021, of which 20,5% patients had primary resistance to hormonal therapy. Symptoms and signs of urinary tract obstruction, such as difficulty urinating, increased urinary frequency, and a feeling of incomplete emptying, were present in most of our patients. Chronic retention and bilateral hydronephrosis with renal insufficiency were observed in 3 patients. Two patients had urinary incontinence due to sphincter infiltration. All possible, routine means of imaging and histological examination of the tumor should be used to determine the development of hormonal resistance of BPH.

Keywords Castration-resistant cancer, Prostate gland, Hormonal resistance, Histological study

1. Introduction

According to the data of Tillashayhov et al. (2021) prostate cancer (BC) makes up 10,0% of malignant neoplasms in general population in the territory of the Republic of Uzbekistan [1,2,7,8]. The variability of the clinical picture of BPH, as well as the frequently occurring asymptomatic course of the disease up to generalization of the process make an early diagnosis of the appearance of resistant BPH difficult [3,5]. The first step in determining hormonal resistance is the fact that conventional methods of hormonal therapy for BPH are unsuccessful.

Hormonal resistance of the tumor in some patients with PCa is determined immediately after the start of treatment, in others it develops after several months of successful treatment with hormonal therapy[4,6]. Despite this, to date, there are no characteristic signs and reliable criteria for determining the primary and secondary forms of hormonal resistance, which complicates the choice of adequate therapy for each patient with BPH [9].

2. Materials and Methods

Received: Jan. 16, 2023; Accepted: Feb. 9, 2023; Published: Feb. 13, 2023
Published online at http://journal.sapub.org/ajmms

Our study was based on data analysis of 112 patients with hormone-resistant prostate cancer (HRPC) under observation in the oncourological department of the RSNPMCRC from 2008 to 2022.

3. Results

Symptoms and signs of urinary tract obstruction, such as difficult urination, increased frequency of urination and feeling of incomplete emptying, were present in most of our patients. Chronic retention and bilateral hydronephrosis with renal insufficiency were observed in 3 patients. Two patients had urinary incontinence due to sphincter infiltration.

Unfortunately, in most patients the first symptoms were moderate pelvic pain and sometimes lumbar pain, which is the result of tumor progression.

One patient had recurrent thrombophlebitis, disseminated intravascular coagulation and bleeding, due to intense bone marrow involvement. In one patient, subclavian adenopathy was the first manifestation of the disease.

The clinical diagnosis of hormone-resistant PCa was established in case of increasing PSA level and/or objective appearance and/or progression of metastases against the background of castrated blood testosterone level. The criteria for this condition were as follows:

- Castration blood testosterone levels (< 50 ng/mL);
- an increase in PSA demonstrated in three consecutive tests performed at least 2 weeks apart, or
- appearance and progression of bone or soft tissue metastases.

There are many works devoted to diagnosis of probable progression of PCa, including occurrence of hormone-resistant forms, by one or other methods of investigation.

All patients of the main and control groups were assessed for the degree of urinary dysfunction according to IPSS (Table 1).

Table 1. Distribution of patients in the main and control groups according to the degree of urinary dysfunction

Scores by degree of urinary dysfunction	Main group		Control group	
	Quantity	%	Quantity	%
Up to 7 points	21	18,8	22	73,3
8 - 19 points	27	24,1	8	26,7
20 points or more	64	57,1	-	-
Total	112	100	30	100

In the main group, more than half of the patients had severe urinary disorders, which required urgent measures to diagnose and treat the patients. Only 18.8% of patients had local disturbances that did not alarm either the patients or the doctors.

In the control group, 26.7% of the patients had some dysuric disorders, which were most likely related to complications of radiation therapy, because all 8 patients had previously received a radical course of radiation therapy. Of the 8, 6 patients began to complain of urinary disorders 1 to 6 months after completion of radiation therapy.

Table 2. Distribution of patients with hormone-resistant PCa according to the stage of the pathological process after detection of hormonal resistance

Stage of the process	G_1	G_2	G_3	G_4	Total
Stage I	1(%)	-	-	-	1 (%)
Stage II	7 (%)	10 (%)	8 (%)	4 (%)	29(%)
Stage III	18 (%)	22(%)	7 (%)	5 (%)	52(%)
Stage IV*	5 (%)	9(%)	9 (%)	7 (%)	30(%)
Total	31 (27,7%)	41 (36,6%)	24 (21,4%)	15 (13,4%)	112 (100%)

**Note - Stage IV - local and locally spread process without/and with distant metastases;*

In addition to dysuric disorders, patients mainly complained of pelvic and lumbosacral pain. In a certain part of patients (24.1%) the process progressed to a certain level without significant symptoms. In these patients the fact of the process progression was established during the next routine examination. At the same time, local progression was registered in 9 patients, and in 18 patients new metastases appeared in lymph nodes (7 patients) and pelvic bone metastases appeared (11 patients). In one case with metastases in the pelvic bone, lung metastases not characteristic of prostate cancer were diagnosed. In the course of the examination, if necessary, we performed restaging of the process (Table 2).

In patients with progressing symptoms of BPH the repeated examinations at different terms after the "completion" of treatment revealed the progression of pathological process in many patients. Out of 7 patients with 1 stage only one had tumor progression from 1 a to 1 b, the rest had progression, in 4 local and in 2 two - distant metastases without a considerable increase of primary volume.

If before the treatment only 58 (51,8%) patients were diagnosed with the highly differentiated tumor forms corresponding to G1-2, then at the moment of resistance 72 (64,3%) patients had already had these degrees of differentiation. In the control group histological analysis was not performed due to complete control of the cancer. The reason for this is the elimination of low differentiated tumor clones under the influence of treatment and accumulation of resistant cell clones.

There are many studies proving the dependence of tumor hormone resistance directly on the type of cells that form it. In all patients with developed hormone resistance we reviewed the primary and histological material obtained during repeated examinations. The preparations for the study were prepared by standard methods of biopsy sample preparation for morphological study. Histological analysis was performed by an experienced, highly qualified physician pathomorphologist, because, most histological forms of BPH resemble acinar adenocarcinoma and have slightly distinguishable morphological features from it. To avoid bias in drawing conclusions, the primary histopreparations were examined separately from the repeat ones. Primary hormone-resistant prostate cancer usually occurs in tumors such as basal cell carcinoma, urothelial prostate cancer, neuroendocrine cancer, and stromal prostate cancer, which occur in the general population of prostate cancer patients at most 5-7%. Secondary resistance occurs in patients with acinar adenocarcinoma and with tubular cancer. The reason for this fact has not yet been fully elucidated.

The conclusions of the comparative analyses (revision of drugs) of the study are shown in Table 3.

Table 3. Results of histological examination of biopsy material in patients with GERD

Conclusion	Primary analysis	Reanalysis
Acinar adenocarcinoma	109 (97,3%)	102 (91,1%)
Basal cell carcinoma	2 (1,8%)	5 (4,7%)
Neuroendocrine cancer	-	-
Tubular cancer	-	1 (0,9%)
Urothelial cancer	1 (0,9%)	4 (3,6%)
Stromal cancer	-	-

4. Conclusions

To date, there is no specific time frame for concluding tumor resistance to hormone therapy after unsuccessful hormone therapy. All possible, routine imaging and histological examinations of the tumor should be used to determine if hormonal resistance has developed.

REFERENCES

[1] Tillyashaikhov M.N. The state of oncological care for the population of the Republic of Uzbekistan Tashkent: IPTD "Uzbekistan", 2021. - 176 p.

[2] Tillyashaykhov M.N., Djanklich S.M., Ibragimov S.N., Imamov O.A. Analysis of cancer incidence structure in the Republic of Uzbekistan. Oncology and Radiology of Kazakhstan, 2021, 61 (3), 4-8.

[3] Buck SAJ, Koolen SLW, Mathijssen RHJ, de Wit R, van Soest RJ. Cross-resistance and drug sequence in prostate cancer. Drug Resistant Update. May 2021; 56: 100761.

[4] Schmidt KT, Huitema ADR, Chau CH, Figg WD. Resistance to second-generation androgen receptor antagonists in prostate cancer. Nat Rev Urol. 2021 Apr; 18(4): 209-226.

[5] Shaxanova Shaxnoza Shavkatovna, Raximov Nodir Maxammatkulovich, Koraboev Fayzullo Tojiboevich, Increase the effectiveness of treatment of multiple osteogenic metastases of kidney and prostate cancer, Journal of reproductive health and uro-nephrology research 2022, vol. 3, issue 2. Pp.

[6] Hamza Abdukodirovich Rakhmanov, Shavkat Erjigitovich Islamov, & Nodir Mukhammadievich Rahimov. (2022). CLINICAL AND MORPHOLOGICAL CHARACTERISTI CS OF PROSTATE CANCER. The American Journal of Medical Sciences and Pharmaceutical Research, 4(02), 17–22. Retrieved from https://inlibrary.uz/index.php/tajmspr/article/view/6171.

[7] Alimjanovich, R. Z., Maxammatkulovich, R. N., & Khikmatovich, K. K. (2022). Age Features of the Prevalence of Prostate Cancer in Uzbekistan. Central Asian Journal of Medical and Natural Science, 3(5), 154-157. Retrieved from https://cajmns.centralasianstudies.org/index.php/CAJMNS/article/view/1062.

[8] Rizaev Jasur, Rakhimov Nodir, Kodyrov Khamidullo, Shakhanova Shakhnoza. Study of prostate cancer death by regions of the republic of Uzbekistan. Journal of Biomedicine and Practice. 2022, vol. 7, issue 5, pp.202-210.

[9] Sh S. S., Raximov N. M. IMPROVING THE COMBINED TREATMENT TACTICS OF MANY OSTEOGEN METASTASES OF MALIGNANT TUMORS OF THE URINARY-BODY SYSTEM // Web of Scientist: International Scientific Research Journal. – 2022. – Т. 3. – №. 4. – С. 1145-1149.