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Application of DNA cytometry in complex assessment of individual disease prognosis

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Received date: December 16, 2019; Accepted date: January 17, 2020; Published date: January 23, 2020

Citation: Cherenkov V. G., Pasevich K. G., Alexandrov A. S. (2020) Application of Dna Cytometry in Complex Assessment of Individual Disease Prognosis. Obstetrics Genecology and Reproductive Sciences, 4(1): DOI:10.31579/2578-8965/033

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Abstract:

1. The results of DNA flow cytometry of prostate cancer samples indicate a large morpho-molecular heterogeneity of the tumor disease. In 40.8% of patients with breast cancer the tumor had a diploid clone and 59.2 – aneuploid, including tetraploid and other variants

2. Further study of the results of DNA cytometry and the accumulation of material in the comprehensive diagnosis of prostate cancer can shed light on the prognosis, clinical course and formation of therapeutic tactics of this pathology.

Key words: prostate cancer; DNA cytometry; prognosis

Prostate cancer (prostate cancer) is one of the leading causes of death in elderly men in most developed countries and is characterized by a very diverse clinical course: from latent slow - flowing , subclinical (incident) clinical forms to rapidly progressive metastatic (occult) forms according to the who classification [2,3]. However, as many authors note, it is very difficult to draw a line between incident and latent prostate cancer, to assess the prognosis. The former are characterized by unpredictability of the disease, quickly metastasize, the latter belong to insignificant long - flowing forms - "patients die with it, but not from it." Even more difficult to distinguish clinical from subclinical forms, is installed accidentally a morphological study of remote adenomas.

With regard to the choice of treatment methods, the available information in the literature is also contradictory: from wait – andsee tactics to combination and complex therapy-radical prostatectomy, radiation therapy and complete androgen blockade. This is largely due to the fact that in many patients, not only the determination of prognostic factors, but also staging is a difficult and far from solved problem.

Currently, the main methods of diagnosis of prostate cancer are:

- - determination of serum prostate-specific antigen (PSA),
- finger rectal examination of the prostate,.
- transrectal ultrasound scan (TRUS).
- He next mandatory stage of examination morphological confirmation of the alleged diagnosis.

The method of choice is transrectal multifocal puncture biopsy of the prostate under ultrasound guidance.

An indicator of morphological verification for the last 10 years, despite some progress, remains low -79,6% [1993-61,7% [1]

Among the currently used prognostic factors and recommendations of the European Association of urologists, the choice of treatment is based on such criteria as age and life expectancy, the prevalence of the process, the level of PSA and the degree of differentiation of the tumor on the Gleason scale [3].

Undoubtedly, these indicators are important for treatment planning, but they often do not provide an answer to predict the development of the disease with the necessary certainty.

It seems promising research aimed at identifying additional biological characteristics of ZN, in particular – to determine the ploidy of tumor cells, proliferative activity, DNA index and other morpho-molecular indicators. In literature works such a plan us not detected

Purpose of Research

The aim of this work is to study the parameters of DNA cytometry of tumor cells in the complex assessment of prognosis and choice of treatment methods.

На каждого больного заведен специально разработанный паспорт с указанием: ФИО п Each patient performed a transrectal multifocal biopsy of the prostate of the six points under ultrasound control. Manipulation was performed with the help of bard Magnum device (needle 18g x 20cm Length, depth of cut 22 mm).

The obtained material was sent to the pathohistological and DNA cytometric laboratories. The study was performed using Becton Dickinson FACSCALIBUR laser flow cytometry. The results were analyzed using the program ModFit LT V. 3. 1, counting the size of cell cycles and the percentage of cells in different phases of the cycle. The

types of DNA histograms were revised according to the models proposed patient, age, PSA level at the time of registration, disease stage, tumor differentiation degree (G), Gleason score, and

testosterone and estradiol levels at the time of registration, tumor cytometry DNA indicators: DNA index, aneuploidy. Many authors argue that prostate cancer is often heterogeneous. [4, 5].

Biological profile of the tumor	Number of patients	Among them: Criterion Gleason			
	(%)	G1	G2	G3	
		(Criterion Gleason 3- 4)	(Criterion Gleason 5-6)	(Criterion Gleason 7- 10)	
Diploid	31(33,7)	7 (22,5%)	14 (45,2%)	10 (32,3%)	
Aneuploid	61(66,3)	8 (13,1%)	21 (34,4%)	32 (52,5%)	
In total	92(100,o)	15	35	42	

Table 1: Biological profile of the tumor. Comparison of ploidy of prostate cancer based on on the degree of differentiation of the tumor

Table 1 shows that most of the group with DNA diploid index has a high and moderate degree of differentiation of tumors G1 and G2 (in total-67.7%). In the aneuploid group, the majority of patients -52.5% of tumors have a low degree of differentiation. It is known that tumors with a low degree of differentiation of tumor cells predict the "aggressive" course of the disease and the early onset of hormone-resistant state in treatment. In the vast majority of these data coincide with the establishment in this group of aneuploid clone of

tumor cells, characterizing the aggressive course of a malignant tumor. At the same time, in the group of patients with low degree of differentiation of tumor cells there is a category of patients with diploid clone (10-32, 34%), as well as Vice versa in the group of patients with aneuploid clone there is a subgroup of patients (8 - 13.1%) with a high degree of differentiation of It can be assumed that the latter can form intermediate variants of both clinical and subclinical course of prostate cancer.

Biological profile	Number of patients	PSA level up to 10 ng / ml	PSA level 10-40 ng / ml	PSA level more than 40 ng / ml
Diploid	31	6 (19,3%)	22 (70,9%)	3 (9,7%)
Aneuploid	61	8 (13,1%)	42 (68,2)	11 (18,1%)
In total	92	14	64	14

 Table 2: Comparative ploidy data depending on the index common prostate specific serum antigen (PSA, Ls.) in patients with prostate cancer stage III-IV disease

s can be seen from table 2, the majority of patients with prostate cancer in the groups with diploid and aneuploid clones had PSA levels of more than 10 ng / ml (81.6% and 86.7%, respectively), which, according to the literature data, is directly related to the total tumor mass of prostate cancer, taking into account metastatic components.

However, according to our observations, the level of PSA has an inverse relationship with the degree of aggressiveness of the tumor. In the course of studies in two patients with aneuploid form of prostate cancer, the presence of multiple metastases in the bones of the skeleton stated extremely low initial

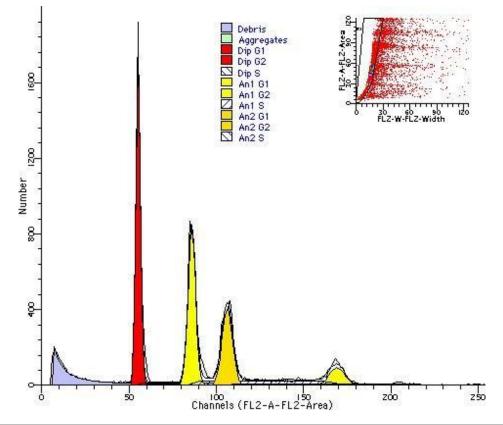


Figure 1: DNA cytometry data of the tumor sample of patient P., 62 g. on the histogram: multiclonal character of the tumor (2 aneuploid DNA clones 42% DI=1.55 and 21% DI=1.92 with high proliferative activity (SPF=22.3%).

PSA level not exceeding 1.0 ng/ml. In these two cases, we believe that we are talking about extremely aggressive forms of cancer, which in the course of their evolution have lost the original specificity of the prostate tissue. This is evidenced by the multiclonal nature of the prostate cancer, which is a tumor focus of several clones (Fig. 1), which, in our opinion, can form both occult and other clinical variants of prostate cancer, which requires further confirmation and accumulation of material.

Conclusion

1. The results of DNA flow cytometry of prostate cancer samples indicate a large morpho-molecular heterogeneity of the tumor disease. In 35, 6% of patients with prostate cancer the tumor had a diploid clone and 64, 4% – aneuploid, including tetraploid and other variants.

2. The highest frequency of bone metastases ($68.4\pm2.9\%$) was found in the anenuploid clone of the tumor, whereas in other variants they did not exceed ($35.7\pm1.5\%$).

3. Further study of the results of DNA cytometry and the accumulation of material in the comprehensive diagnosis of prostate cancer can shed light on the prognosis, clinical course and formation of therapeutic tactics of this pathology.

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DOI:10.31579/2578-8965/033

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