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Research Article

CLINICAL AND MORPHOLOGICAL CHARACTERISTICS OF PROSTATE CANCER

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ABSTRACT

The article highlights clinical and morphological characteristics of prostate cancer. The results of the carried out researches at the character study, pathogenesis of the development and diagnostics testify to the increase of number of so called "hormone-resistant" cases of the prostate cancer. It has been established that morphological diagnosis of prostate cancer is difficult, because signs of malignancy may be barely visible, which increases the probability of a false-negative result. At the same time there are many benign processes that mimic a malignant tumour, which can lead to misdiagnosis. In recent years, the use of immunohistological markers to detect basal layer cells has been recommended. Their level can be determined by immunohistochemical examination, which is elevated in prostate cancer.

KEYWORDS

Prostate cancer, clinic, morphology, diagnosis.

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INTRODUCTION

Prostate cancer remains the most frequent solid tumour in American and European men. There are an estimated 250,000 new cases of this disease in the United States each year and approximately 30,000 men die from it .

With the widespread introduction of prostate specific antigen detection, the frequency of diagnosis of localized and locally advanced stages of prostate cancer has increased considerably. In Europe and the USA, non-palpable stages of prostate cancer account for 75% of detected cases. The results of the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO) and the European Randomized Study of Screening for Prostate Cancer are presented. Based on the initial results of the studies, antigen-based screening can reduce prostate cancer mortality by approximately 20%, but leads to a risk of detecting clinically insignificant masses. It has been noted that a differentiated approach to newly diagnosed cases of pathology is needed, assessing the individual risks of the patient.

PURPOSE OF THE RESEARCH

To establish clinical and morphological characteristics of prostate cancer.

MATERIAL AND METHODS OF THE RESEARCH

As objects we studied living patients with prostate cancer who were hospitalized in Samarkand regional branch of the Republican Specialized Scientific-Practical Medical Center of Oncology and Radiology (20), analyzed their medical documents (case records), as well as the results of clinical and laboratory investigations, data of morphological studies. We took into account the results of follow-up, macroscopic, microscopic (hematoxylin and eosin staining), morphometric and statistical research methods.

RESULTS OF THE STUDY AND THEIR DISCUSSION

Clinical signs: In most men with adenocarcinoma (T1a) incidentally detected by transurethral resection of the prostate, the process does not progress for 10 years or more. In this case, only dynamic monitoring is necessary for older patients, while younger men with a longer life expectancy may require needle biopsy to rule out a malignancy in the periphery of the prostate. Tib tumors are more dangerous. They are treated in the same way as tumors identified by needle biopsy, because they are fatal in 20% of cases without treatment.

Localized prostate cancer is asymptomatic and usually appears as a nodule on rectal palpation or if the PSA level in the serum {prostate specific antigen} is elevated. Prostate cancer usually originates in the periphery away from the urethra, and therefore urinary disorders are only seen at a late stage.

Clinical manifestations of prostate cancer include difficulty in beginning to urinate or interruption of the flow of urine, dysuria, rapid urination, or hematuria. It is now rare for patients to complain of low back pain caused by metastases to the spine. Detection of osteoblastic metastases on review radiographs or with more sensitive radioisotope bone scans allows a diagnosis of prostate cancer. These patients have an unequivocally unfavorable prognosis.

The rectal finger examination can detect carcinoma at an early stage if it is localized posteriorly (but this method has low sensitivity and specificity). Transrectal ultrasound (USG) and other imaging modalities reveal characteristic signs of prostate cancer, but the low

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sensitivity and specificity of these methods also limit their use in practice. Transrectal needle biopsy of the prostate gland is usually necessary to confirm the diagnosis.

The PSA test is the most important test in the diagnosis of prostate cancer and the evaluation of the efficacy of treatment (6). PSA is formed in the epithelial cells of the prostate gland and is normally secreted into the seminal fluid. PSA is a serine protease whose main task is to keep the semen fluid after ejaculation. Normally, men have very low plasma PSA concentrations. Elevated PSA levels can be caused by either localized or advanced malignancy. Most laboratories consider a PSA level of 4 ng/ml to be a borderline value. However, this approach to PSA level determination is not accurate, which may cause a delay in the diagnosis of prostate cancer.

PSA is a specific marker for an organ, but not for cancer. Factors such as prostatitis, heart attack, instrumental prostate exams, and ejaculation can also contribute to an elevated PSA. Moreover, 20-40% of patients with localized prostate cancer have PSA concentrations of 4 ng/ml or lower.

The PSA test is so detailed because it is ubiquitous, and because it is difficult and prone to misinterpretation. In fact, the PSA test is a test to detect malignancy. Consequently, physicians should ensure that test results are returned from the laboratory, that PSA values that differ from normal are recorded, and that patients are called in for consultation if their levels of this antigen are elevated. Most medical errors are the result of underestimating PSA levels and thus causing a delayed diagnosis of malignancy.

Morphology : In 70% of cases, carcinoma of the prostate gland is localized in its peripheral zone (usually in the posterior part of the gland, which allows to palpate the tumor during rectal finger examination). It is characteristic that on the section of the gland the tumor tissue is granular and dense. If a tumor is located in the prostate gland tissue, it is poorly visualized, but easier to detect by palpation. Local spreading usually involves the periprostatic tissue, the seminal vesicles, and the base of the bladder, which in advanced forms may lead to urethral obstruction. Metastases first spread through the lymphatic vessels to the level of the obstructing lymph nodes and reach the para-aortic lymph nodes. Hematogenous dissemination occurs mainly in bone, especially in the bones of the axial skeleton, but in some cases there is massive dissemination to internal organs (the exception rather than the rule). Bone metastases are usually osteoblasts and, if found in men, clearly indicate the presence of prostate cancer. The most frequently affected area is the lumbar spine, followed (in descending order of frequency) by the proximal femur, pelvic bones, thoracic spine, and ribs.

Histologically, most prostatic tumors are adenocarcinomas, which are characterized by well-defined, easily defined glandular structures. Tumor glands are usually smaller in size and lined by a single layer of cubic cells or by low cylindrical epithelial cells. Tumor glands are located closer to each other and, characteristically, lack branching or papillary invaginations. Tumor glands lack external basal layer typical for glands of normal organ. Cytoplasm of tumor cells varies from dull-light, typical for cells of unchanged glands, to distinctly amphophilic. The nuclei are large and often contain one or more large nuclei. There are some differences in the size of nuclei and their shape, but on the whole, pleomorphism is not very pronounced. Figures of mitosis are uncharacteristic.

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The diagnosis of prostate cancer represents one of the greatest challenges for the anatomical pathologist. The problem is not only the insufficient amount of tissue obtained during needle biopsy for histological examination, but also the fact that often the biopsy specimens contain only a few tumor glands among many normal ones (Fig. 1). Morphological diagnosis of prostate cancer is also difficult because signs of malignancy can be subtle, which increases the chance of a false negative result. There are also many benign processes that mimic a malignant tumor, which can also lead to misdiagnosis. Although there are several histological features specific to prostate cancer, such as perineural invasion, the diagnosis is made when a combination of tissue, cellular, and some additional features are present. As noted earlier, the main distinguishing feature of a benign process in the prostate is the presence of cells in the basal layer, whereas their absence is indicative of prostate cancer (Fig. 1) .

Pathologists use this peculiarity by using immunohistological markers to detect cells of the basal layer. Immunohistochemical testing can be used to determine the level of AMACR, which is elevated in prostate cancer. The majority of malignant tumors of the prostate give a positive reaction to AMACR. The sensitivity of this method varies from 82 to 100%. The use of these markers to increase the accuracy of prostate cancer diagnosis has its limitations because of the possibility of false-positive and false-negative results; therefore, routine hematoxylin and eosin staining should also be performed.

In = 80% of cases, high grade PIN is also found in prostate tissue with carcinoma. PIN is characterized by the presence of normal prostate glands lined by atypical cells with pronounced nuclei. Cytologically, PIN and carcinoma may be identical, but on the tissue level, PIN is characterized by larger branching glands with papillary overgrowths in contrast to invasive cancer, in which small glands with smooth lumen boundaries are closely spaced.

The glands of PIN are lined by a discontinuous basal layer and an unchanged basal membrane. PIN and invasive cancer have several features in common. First, they localize predominantly in the peripheral zone. If we compare the prostate gland affected and unaffected by a malignant tumor, PIN is more often found in the prostate gland with a tumor. PIN is usually located in close proximity to the malignant tumor, and in some cases is transformed into it. Most of the molecular changes characteristic of invasive cancer are also present in PIN, confirming the fact that PIN is a transitional link between unaltered tissue and invasive cancer. However, the cause of PIN and how often it transforms into cancer is still unknown, so the term "carcinoma in situ" is not applicable to PIN (unlike cervical cancer).

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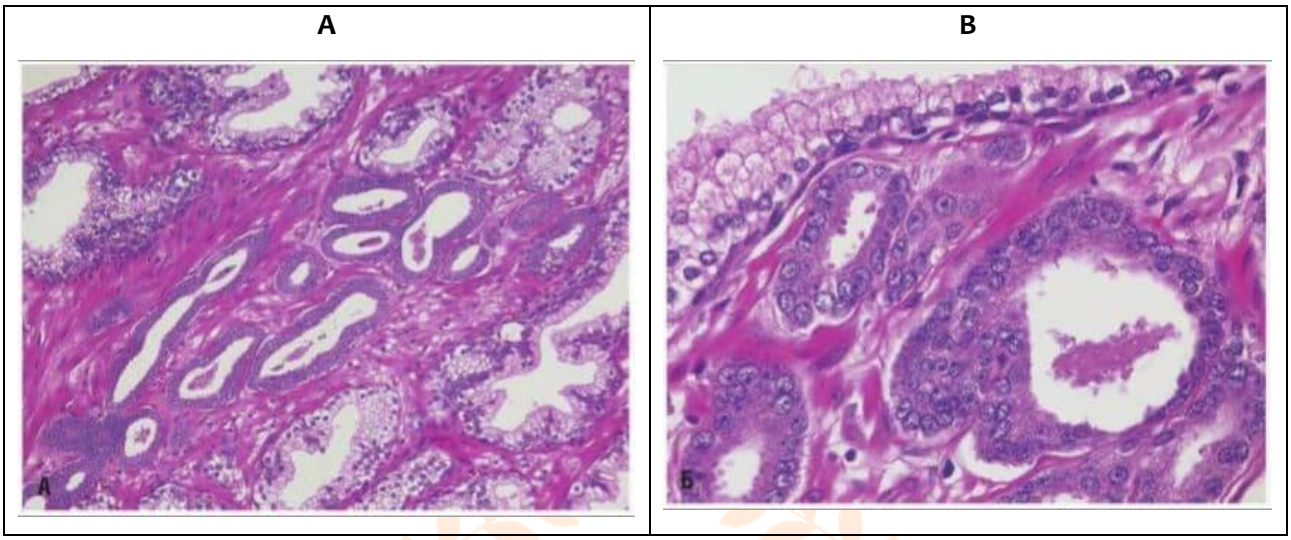

Fig. 1. (A) Adenocarcinoma of the prostate characterized by small tumor glands arranged in groups between larger normal glands. (B) Several small tumor glands characterized by enlarged nuclei, prominent nuclei, and dark cytoplasm are seen under high magnification (top)

Repeated measurements of PSA levels are very important in evaluating the effectiveness of therapy. For example, elevated PSA levels after radical prostatectomy or radiation therapy for localized cancer indicate recurrence or dissemination of tumor cells. Detection of PSA by immunohistochemical examination in samples of prostate tissue can also help a pathologist to establish the presence of a metastatic tumor in the prostate [6].

Surgical method, radiation therapy, and hormonal therapy are used for treatment of prostate cancer. Life expectancy for more than 90% of patients receiving this treatment is about 15 years. Currently, the most common method of treatment for localized prostate cancer is a radical prostatectomy. Its prognosis depends on the stage of the disease, the condition of the tissue at the border of the resection, and the degree of Gleason malignancy. An alternative method of treating localized prostate cancer is distant or intradermal radiotherapy, which consists of placing radioactive sources of radiation (brachytherapy) into the prostate tissue. Radiation therapy is also used to treat localized tumors that are too small to be treated by surgery.

Hormone therapy in patients with No stage did not improve the results of surgical treatment . Hormone therapy in patients with locally advanced disease (T3) did not reduce the risk of tumor cells at the incision margin.

Because some prostate tumors are characterized by a relatively asymptomatic course, it can take up to 10 years before the benefits of surgery or radiation therapy can be evaluated. Because of this, active surveillance may be recommended for most older men, men with significant comorbidities, and even some younger men with low PSA levels and locally highly differentiated prostate cancer.

Prayer-Galetti T. et al. conducted a prospective randomized study that included 201 patients with stage C prostate cancer and revealed that adjuvant hormone therapy with gonadotropin-releasing hormone agonist goserelin (zoladex) in a dose of 3.6 mg subcutaneously every 28 days after radical prostatectomy significantly

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increases recurrence-free survival compared to surgical treatment alone in high risk prostate cancer patients.

Treatment of advanced metastatic carcinoma of the prostate is based on the removal of androgen exposure through orchiectomy or by taking synthetic luteinizing hormone (LH) releasing factor agonists. Prolonged use of these agonists leads to a state of drug castration. However, although anti-androgen therapy leads to remission, the tumor eventually becomes resistant to testosterone, after which it rapidly progresses to death.

CONCLUSIONS

The obtained results of the research testify to the fact that the clinical and morphological criteria of the prostate cancer are incompletely developed. Thus there is an increase of so called "hormone resistant" prostate cancer cases. At the same time morphological diagnostics of prostate cancer is difficult because the signs of malignancy can be hardly visible, which increases the probability of false negative result. There are also many benign processes that mimic a malignant tumor, which can also lead to misdiagnosis. In recent years, the use of immunohistologic markers to detect basal layer cells has been recommended. With the help of immunohistochemical study it is possible to determine their level, which is increased in prostate cancer.

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