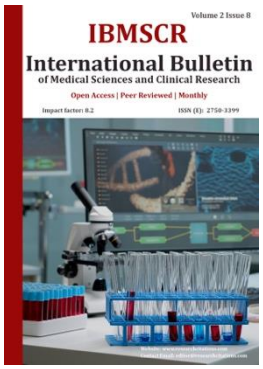

PROSTATE CANCER: PATHOLOGY AND TREATMENT

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Abstract

Prostate cancer is a major public health problem throughout the developed world. For patients with clinically localised prostate cancer, the diagnosis is typically established by histopathological examination of prostate needle biopsy samples. Major and minor criteria are used to establish the diagnosis, based on the microscopic appearance of slides stained using haematoxylin and eosin.The incidence of prostate cancer shows strong age, race, and geographical dependence. Less than 2% of cases are diagnosed under the age of 41, although this may represent an underestimate as screening for disease in young men is rare. Prostate cancer is relatively uncommon in Asian populations and prevalent in Scandinavian countries, and the highest incidence (and mortality) rates known are in African Americans. Causes of the disease are essentially unknown, although hormonal factors are involved, and diet may exert an indirect influence; some genes, potentially involved in hereditary prostate cancer (HPC) have been identified. A suspect of prostate cancer may derive from elevated serum prostate-specific antigen (PSA) values and suspicious digital rectal examination (DRE) finding.

For a definitive diagnosis, however, a positive prostate biopsy is requested. Treatment strategy is defined according to initial PSA stage, and grade of the disease and age and general conditions of the patient.

Key Words: prostate-specific antigen (PSA), hereditary prostate cancer (HPC), Gleason system, pathological stage(pTNM), low urinary tract symptoms (LUTS), transrectal ultrasonography (TRUS), digital rectal examination (DRE), hormone-refractory prostate cancer (HRPC).

Epidemiology

Epidemiologic studies have found no consistent correlation of prostatic cancer with diet, venereal disease, sexual habits, smoking, or occupational exposure.However, higher serum testosterone levels have been proposed as a major determinant of the risk of prostatic cancer.

In Europe, during the early 2000s the relative survival rate at 7 years after diagnosis of prostate cancer was 70%. Survival increased slightly with age from 59% in the youngest (<58 years) to 74% in the older age group of patients (67–76 years), and then fell to 55% for the oldest group of 85 years old or more. During the period 1990–98, 8-year survival significantly increased from 57 to 70%.

Pathology

About 75–80% of prostate cancers arise in the peripheral zone of the gland, mainly in a

posterior location, of the remaining cases, 20% derive from the central zone and 15–20% from the transitional zone.

Prostate adenocarcinoma may spread locally, by direct invasion of seminal vesicles, urinary bladder or surrounding tissues or distantly.

The Gleason system is the most widely used grading system for prostate cancer (adenocarcinoma only). Prostate cancers are stratified into five grades (1–5) on the basis of the glandular pattern and degree of differentiation.The Gleason system can be applied to biopsy and surgical specimens, but not to fine needle biopsy (FNB), which lack architectural data. The pathology report following radical prostatectomy should include the extent of tumour involvement, presence and site of eventual positive margins, presence of eventual extension through the capsule and involvement of seminal vesicles, number and site of resected lymph nodes with or without eventual metastases, primary, secondary Gleason grades and definitive Gleason score, expression of pathological stage(pTNM).

Diagnosis

Low urinary tract symptoms (LUTS) can be present in
organ-confined tumors but are usually due to concomitant
benign prostatic hyperplasia (BPH). Locally advanced disease, however, is more likely to have an increase in LUTS
due both to BPH and carcinoma.

A diagnosis of prostate cancer may be suspected from
symptoms, a suspicious digital rectal examination (DRE)
finding or an elevated serum prostate-specific antigen
value. A definitive diagnosis, however, demands the presence
of a positive prostate biopsy. DRE can be utilized to detect suspected tumors, since the majority of cancers are located in the posterior zone.

Serum PSA, DRE and transrectal ultrasonography
(TRUS) constitute the three major diagnostic means for the detection of cancer.

A significant risk of detecting clinically insignificant cancers with this procedure in patients with low PSA levels has to be remembered. Numerous modifications have been suggested to improve both PSA specificity and early detection, particularly in the range 4–10 ng/ml PSA velocity and PSA doubling time, age-specific reference ranges, PSA density and PSA density of the transition zone, PSA molecular forms. Biopsy has to be repeated in men with persistently elevated serum PSA and a negative initial biopsy (detection rate of about 25%).

Treatment

Treatment strategy is defined according to initial PSA, stage and grade of the disease and to the age and general conditions of the patient. Watchful waiting (WW), surgery and radiotherapy could be appropriate choices for patients with localized disease, while hormone-therapy plus radiotherapy should be considered treatment of choice for locally advanced or bulky disease. In cases of advanced disease, ablative hormone-therapy remains the mainstay of treatment while chemotherapy has to be evaluated in patients with hormone-refractory prostate cancer (HRPC). Watchful waiting is indicated as primary option for patients with well or moderately differentiated clinically localized tumours and a life expectancy of less than 15 years. Radical prostatectomy (characterized by the removal of the entire prostate gland with seminal vesicles and lymphnode resection) is currently the most common treatment option in young patients with organ confined prostate cancer.

Published studies have shown a significant decrease in the positive margin rate after neoadjuvant androgen deprivation (probably due to an increased difficulty in determining e accurately the tumor at the inked margin).Alternative approaches for treatment of local recurrencies after radiation therapy, such as cryosurgical ablation or high focused ultrasound (Hi-FU), are still under clinical evaluation.

The treatment of choice for advanced prostate cancer is androgen ablation, achieved via surgical (bilateral orchiectomy) or medical (LH–RH analogues) castration, which is effective, but not curative in 82–88% of cases.

Conclusions

The dilemma of prostate cancer presents the clinician and basic researcher with a number of challenges somewhat unique in human oncology. Its frequent occurrence, tendency for a long natural history, common multifocality and morphologic heterogeneity, and progression to hormone refractory state are all poorly understood aspects of this disease.Treatment strategy is defined according to initial PSA stage, and grade of the disease and age and general conditions of the patient. In cases of advanced disease, ablative hormone-therapy remains the mainstay of treatment while chemotherapy has to be evaluated in patients with hormone-refractory prostate cancer.

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