REVIEW ARTICLE

Prostate Cancer and New Treatment Options

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ABSTRACT

The prostate is a chestnut-sized gland located just below the bladder, behind the pubic bone, and in front of the end of the colon. The basic function of the prostate gland is to produce most of the fluid in the semen. The fluid (secretion) of the prostate and seminal vesicles protects and nourishes the sperm on their way to the ovum of a woman in the womb. The basic function of the prostate is related to fertility, not the sexual power of a man. The most common changes in the prostate gland are inflammation (prostatitis) and benign prostatic hyperplasia. New treatment options for prostate cancer are highlighted.

Key words: Bladder, cancer, health, prostate

INTRODUCTION

Urological disorders account for about one-third of all surgical admissions to hospital.[1] Urological pathology is also a common reason for patients to present in primary care. Although few urological conditions are immediately life threatening, many may have a profound effect on the patient's quality of life.

As with all other medical and surgical specialties, subspecialization has occurred within the urological practice. Evidence in the confidential inquiry into perioperative deaths highlighted that transurethral prostatectomy, the operation performed most often in urological departments, is associated with significantly lower mortality when performed by surgeons who undertake more than 50 such procedures a year. Most urologists will undertake core urology and will subspecialize in one or two of the component parts of urology. One common theme is that urological surgery requires specialized urological nursing to be effective.

BLADDER

Prostate and bladder cancer are the two most common malignant diseases that present to urologists.[1] The numbers of renal and testicular cancers that are being found seem to be increasing. All patients with malignant diseases now come under the care of a multidisciplinary team that consists of urologists, oncologists, radiologists, and histopathologists. Urological oncologist nurses have an increasing role to play in the counseling and follow-up of patients with malignant disease.

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Problems of bladder outflow obstruction secondary to benign prostatic hyperplasia (BPH) constitute about one-third of cases in urological practice. Other urodynamic disorders occur in patients with neurological disorders of many kinds. The management of patients with urinary incontinence may also be included under this heading, although urogynecologists are now taking over a considerable part of this workload.

BLADDER OUTFLOW OBSTRUCTION

Bladder outflow obstruction is most commonly the result of benign prostatic hyperplasia, which expands the transition zone of the prostate.[2] This is a part of the normal aging process, and 10% of men in their 40s and up to 90% of men aged ≥80 years will have symptoms that are attributed to benign prostatic hyperplasia. Other causes of bladder outflow obstruction include urethral stricture, bladder neck obstruction, and bladder neck dyssynergia.

The assessment of a man with bladder outflow obstruction begins with a history. Conventionally, symptoms have been divided into irritative (related to storage of urine) and obstructive (voiding symptoms). The severity of symptoms can be quantified by the use of numerical symptoms scoring sheets such as the International Prostate Symptom Score.

Urine should be sent for microscopy and culture to exclude a urinary tract infection. Hematuria should alert the doctor to other urological pathology that requires further evaluation. Serum electrolytes should also be requested. After discussion with the patient, an assay for prostate-specific antigen should be requested, although this remains controversial.

Prostate-specific antigen is a glycoprotein that is secreted by the epithelial cells that line the prostatic acini. Any

disease process that interferes with the basement membrane of these cells will result in elevated levels of prostate-specific antigen.

One of the most important investigations in patients suspected of having bladder outflow obstruction is a measurement of the rate of urine flow and the volume of residual urine after the bladder is emptied. Normal bladder filling occurs up to a volume of 300–500 ml. The normal bladder, in the absence of outlet obstruction, empties to completion with a maximum flow rate of >15 ml/s. A poor flow rate is not proof of obstruction as a similar picture can be caused by detrusor failure.

PROSTATE

To avoid causing the patient discomfort, rectal examination is performed best with the patient in the left lateral position.[3] The examiner's finger should be inserted while the patient exhales to encourage maximum relaxation of the anal sphincter. The tone of the anal sphincter is noted, and in patients with incontinence as a result of weakness of the sphincter, it is helpful to ask the patient to contract their anal sphincter. Perianal sensation can be tested in the distribution of the S2, S3, and S4 segments – the spinal segments responsible for the main motor and sensory innervation of the bladder.

Examination of the prostate per rectum provides only a rough estimate of the size: The prostate can be categorized as small, medium, or large. The consistency of the prostate can be described as soft, firm, or hard; the surface as smooth or irregular; and the lateral lobes as symmetrical or asymmetrical. Although malignant prostates classically are hard, no precise correlation exists between any of the features described and a specific pathology. Although patients find examination of the prostate uncomfortable, only a bad examination technique, anal pathology, or inflamed prostate will cause significant discomfort or pain.

CANCER

Prostate cancer results from a complex and yet unclear interaction between aging, genetic factors, hormones, growth factors, and the environment, including an increasing body of evidence incriminating dietary fat.[4]

Prostate cancer can be sporadic: Familial with clustering of disease within families and exposure to common risk factors or hereditary, with typical characteristics of early age onset and an autosomal dominant inheritance pattern. The latter is likely to be triggered by a single gene passed along families, yet to be discovered and possibly located in chromosome 1. It has been estimated that men who have three first-degree relatives have a 10.9-fold increase in risk of developing the disease. An increased risk of prostate cancer has also been associated with familial breast cancer. It is generally accepted that prostate cancer is not divided into latent and clinically significant tumor, but it is a very long natural history, coupled with cumulative genetic and biological changes, eventually leads to progressive disease. It is the length of this natural history that allows more men to die with the disease than from it.

As with any tumor, prostate cancers are described in terms of their grade and stage.[5] The grade relates to the appearance of the cancer cells, as compared with that of the normal parent prostate tissue. The grade varies from low, with appearance similar to prostate cells, to high, with totally rogue cells. It is usual to attempt to quantify the degree of cellular change using a so-called Gleason classification. This measures a level of cellular differentiation between 1 and 10, with a worsening of grade in the higher numbers.

The stage of a tumor is defined by its local extension and, if present, metastatic spread. Prostate cancer will arise within one or other lobe of the prostate and then spread, initially, to the capsular rim and then beyond. Early spread beyond the capsule will involve the adjacent tissues of the pelvis. Spread through the lymphatic ducts is, initially, into the pelvic lymph nodes. Spread may also occur through the bloodstream into distant parts of the body. Bone and, in particular, the bone in the pelvis and spine are the most common sites for secondary metastatic prostate cancer. The clinical stage of localized prostate cancer can be detected by rectal examination. This is a reasonably effective assessment of localized prostate cancer. More detailed assessment of prostate cancer is defined by a transrectal ultrasound scan. This examination is often associated with a guided needle biopsy of the prostate. The biopsy, so obtained, is used to confirm the diagnosis of prostate cancer and, if positive, give information on its grade. Computed tomography (CT) scanning of the abdomen and pelvis to check for lymph node spread and a bone scan to check for bony metastases are important additional aids in the detection of metastatic disease in the assessment of tumor stage.

Early prostate cancer produces no specific symptoms, so most men present with lower urinary tract symptoms of benign prostatic hyperplasia.[6] About 10% of patients who undergo surgery for benign prostatic hyperplasia will be found to have prostate cancer after histological examination of the prostate.

Men referred with lower urinary tract symptoms should undergo a full history and clinical examination. The latter

should always include digital rectal examination of the prostate.

Many urological departments have started to use age-specific reference ranges for levels of prostate-specific antigen rather than absolute cutoff values for normal or abnormal levels. The use of these age-specific reference ranges may detect prostate cancer at an early stage in younger men and reduce the number of unnecessary biopsies in older men.

The standard test for prostate-specific antigen measures the total amount of the antigen in the bloodstream, but it exists in different states. Most prostate-specific antigen in serum is bound to protein, but a proportion exists free in the bloodstream. The proportion of free prostate-specific antigen reduces in patients with prostate cancer. The proportion of free prostate-specific antigen can be measured, and this can be expressed as a ratio of the level of total prostate-specific antigen. A free to total prostate-specific antigen ratio of <25% in men with a total level of 4–10 ng/ml has been shown to detect 95% of cancers while avoiding 20% of unnecessary biopsies.

MANAGEMENT

Before a decision can be made about management, the cancer must be staged with the tumor, node, and metastasis classification system and given a Gleason score.[6] Most prostate cancers are heterogeneous, and various degrees of histological differentiation will be seen down the microscope. The two most common patterns are given a score of 1–5 (with 5 being the most poorly differentiated). This is expressed most commonly as, for example, “Gleason 4 + 3.”

CT and magnetic resonance imaging are often used to stage prostate cancer to determine the presence of extracapsular spread or distant metastasis, which might preclude intervention with radical therapy.

Studies, however, have shown that these imaging methods may be of limited value. The resolution of CT is too low to be able to distinguish abnormalities within the prostate gland, the state of the prostatic capsule, or the presence or absence of disease outside the prostate gland. Magnetic resonance imaging seems to be of limited value overall in clinically localized prostate cancer. The use of an endorectal magnetic resonance coil can help predict extracapsular penetration or involvement of the seminal vesicles. CT and magnetic resonance imaging, however, may have a role in evaluating the status of lymph nodes in patients at risk of involvement of the lymph nodes, who are suitable for radical surgery or radiotherapy.

CHEMOPREVENTION

Prostate cancer is a leading cause of cancer and cancer death in American men. For the year 2008, 186,000 prostate cancer cases were expected and 28,700 deaths due to this disease.[7] In the United States, there is an overall 16.7% risk of developing prostate cancer, and early detection and treatment remain the primary focus for controlling the disease. More than 90% of men diagnosed with prostate cancer currently opt for treatment. This increasing incidence of prostate cancer, the morbidity and mortality of the disease and its treatments combined with an improved insight into its biological basis and hormone dependency, has led to an increasing interest in chemoprevention strategies.

Chemoprevention refers to the use of agents to prevent cancer or the adverse outcomes of the disease. Multiple factors, including high incidence, long latency period between initial evidence of prostate cancer and the development of overt or lethal disease, and advanced age of onset and death, make prostate cancer an ideal target for chemoprevention strategies. Even a modest delay in the development of symptomatic cancer may be sufficient to reduce the incidence of the disease, improve survival, and prevent the complications of the disease and the morbidity of its treatments.

NEW THERAPIES

New research on gene changes linked to prostate cancer is helping scientists better understand how prostate cancer develops.[8] This could make it possible to design medicines to target those changes. Tests for abnormal prostate cancer genes might also help identify men at high risk who might benefit from screening or from chemoprevention clinical trials, which use drugs to try to keep them from getting cancer. In men already diagnosed with prostate cancer, tests for certain gene changes can give men and their doctors a better idea of how likely the cancer is to grow and spread, which might influence treatment options.

Advances in technology are making it possible to aim radiation more precisely than in the past. Current methods such as conformal radiation therapy, intensity-modulated radiation therapy, and proton beam radiation help doctors avoid giving radiation to normal tissues as much as possible. These methods are expected to increase the effectiveness of radiation therapy while reducing the side effects. Technology is making other forms of radiation therapy more effective as well. New computer programs allow doctors to better plan the radiation doses and approaches for both external radiation therapy and brachytherapy. Planning

for brachytherapy can now even be done during the procedure (intraoperatively).

Researchers are looking at newer forms of treatment for early-stage prostate cancer. These new treatments could be used either as the first type of treatment or after unsuccessful radiation therapy. One treatment, known as high-intensity focused ultrasound, destroys cancer cells by heating them with highly focused ultrasonic beams. This treatment has been used in some countries for a while and is now available in the United States. Its safety and effectiveness are now being studied, although most doctors in the US do not consider it to be a proven first-line treatment for prostate cancer at this time.

CONCLUSION

Prostate cancer is a malignant tumor that develops in the prostate gland and can eventually spread to other organs and tissues through blood and lymph. Fortunately, prostate cancer is generally growing at a slower rate than many other cancers. Almost 90% of all prostate cancers remain clinically unnoticed for decades. Such a high incidence of clinically undetectable or accidentally detected malignancy is a unique feature of prostate cancer. The exact cause of prostate cancer is unknown. It is not thought to be related to BPH. Risk factors for prostate cancer are advanced age, genetics, hormonal influences, and environmental factors such as toxins, chemicals, and industrial products.

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