Clinical Management of

Prostatic Cancer

Joseph A. Smith, Jr.
Richard G. Middleton

Clinical Management of Prostatic Cancer

JOSEPH A. SMITH, JR., M.D.
Associate Professor
Division of Urology
Department of Surgery
University of Utah School of Medicine
Salt Lake City, Utah

RICHARD G. MIDDLETON, M.D.
Chairman, Division of Urology
University of Utah School of Medicine
Salt Lake City, Utah

YEAR BOOK MEDICAL PUBLISHERS, INC.
Chicago • London • Boca Raton

Printed in the United States of America.

1 2 3 4 5 6 7 8 9 0 KC 91 90 89 88 87

Library of Congress Cataloging-in-Publication Data

Smith, Joseph A., 1949–
Clinical management of prostatic cancer.

Includes bibliographies and index.
1. Prostate gland—Cancer. I. Middleton, Richard G.
II. Title. [DNLM: 1. Prostatic Neoplasms—therapy.
WJ 752 S651c]
RC280.P7S65 1987 616.99′463 87-6129
ISBN 0-8151-7843-3

Sponsoring Editor: Daniel J. Doody
Manager, Copyediting Services: Frances M. Perveiler
Production Project Manager: Carol A. Reynolds
Proofroom Supervisor: Shirley E. Taylor

Clinical Management of Prostatic Cancer

Titles of Related Interest

Soloway, Hardeman/*Clinical Management of Bladder Cancer*
Publication 1989

Other titles under development:

Clinical Management of Testicular Cancer
Clinical Management of Renal (Cell) Cancer

Preface

The subject of prostatic cancer has been addressed extensively in the medical literature. To a great extent, interest has been prompted by the frequency of the disease as well as the intriguing and unpredictable natural history of prostatic cancer in an individual patient. In addition, the large body of printed literature as well as verbal discussion generated by carcinoma of the prostate have emerged because of the strikingly different—and often opposing—viewpoints regarding appropriate treatment in a given clinical situation. Because of this, the clinician frequently is both frustrated and confused in attempting to make clinical decisions or treatment recommendations for patients with prostatic cancer.

It is not the purpose of this book to review exhaustively the literature on prostatic cancer or simply to reproduce information that is otherwise easily obtainable. Rather, an attempt is made to present practical, reasonable recommendations based on extensive clinical experience as well as interpretation of the pertinent literature. Thus, this book is intended for all clinicians involved in the treatment of patients with prostatic cancer.

Considering the confusing and sometimes contradictory data that have been generated regarding prostatic cancer, dogmatic treatment recommendations frequently are unfounded and often reflect a poor understanding of the disease. Therefore, alternative treatment approaches are acknowledged as much as possible. To a great extent, therapeutic recommendations should be based on efforts to select patients most likely to benefit from a given form of treatment, while sparing treatment expense and morbidity in those patients unlikely to respond or not in need of treatment.

Inevitably, some of our biases emerge through some of the treatment recommendations. Clinical biases cannot be completely subdued but should be based as much as possible upon an impartial and objective interpretation of available information as well as application of these data to the circumstances of an individual situation. A simple presentation of facts and "letting the patient make the choice" is impractical and often unfair to patients. Although patient wishes are paramount in deciding upon treatment, the very basis of clinical

skill is to weigh the advantages and disadvantages of a given treatment and present the options and recommendations to a patient in a meaningful manner. In this way, the most appropriate treatment in terms of both therapeutic efficacy and treatment morbidity can be determined for an individual patient.

Sincere appreciation is expressed to Marcia Thompson for her usual excellent work in the preparation of this text.

JOSEPH A. SMITH, JR., M.D.
RICHARD G. MIDDLETON, M.D.

Contents

1

Detection and Diagnosis

EPIDEMIOLOGY

In the United States and many European countries, carcinoma of the prostate is the second most common cancer and the third leading cause of cancer death in men. In the United States alone, it is estimated by the American Cancer Society that there will be 90,000 new cases of prostatic cancer in 1986 and 26,000 deaths.[1] Although the etiology of prostatic cancer is unknown, some contributing factors to the development of the disease have been defined as well as some dominant epidemiologic patterns. A general knowledge of these factors is important for the clinician treating patients with prostatic cancer because it may help identify individual patients or segments of the population at large who may be at greater risk and require more careful screening or follow-up.

Age

The association between prostatic cancer and increasing age is well recognized and striking. Unlike most cancers which may have a peak age of incidence, the incidence and prevalence of prostatic cancer continue to increase with advancing age. Autopsy studies have shown histologic evidence of prostatic cancer in over 40% of men whose death occurs in the ninth decade.[2]

Equally impressive is the low incidence of the disease below age 50 or 55. Prostatic cancer is a rare disease in younger men. In general, it is recommended that yearly rectal examination for screening of prostatic cancer begin at age 50 in most men. A widespread clinical impression among physicians treating prostatic cancer is that the disease is more virulent and rapidly progressive in younger men. Although statistical studies do not necessarily verify this impression on a stage-for-stage basis, they do indicate that metastatic disease is found more often at the time of presentation in younger men than in older age groups.[3] Finally, it is anticipated that the disease will have a clinically significant impact or eventually be the cause of death for a greater percentage of younger men in whom longevity would otherwise be greater.

Race

In epidemiologic studies of cancer, it is difficult to separate racial factors from other influences. Culture, diet, and environment vary among ethnic or racial groups even within the same country. Nevertheless, there are striking differences in the incidence of prostatic cancer that are notable on a worldwide basis and among ethnic groups within the same country. Curiously, most studies suggest that the prevalence of clinically occult prostatic cancer found at autopsy is similar throughout all countries and racial groups.[4] However, the rates of clinically apparent disease and prostatic cancer mortality vary widely.

The highest incidence of age-adjusted death rate from prostatic cancer is found in Scandinavian countries (Fig 1–1). The United States has an incidence similar to that of most Northern European countries, whereas rates are somewhat lower in Israel, southern Europe, and South America. The lowest reported incidence of prostatic cancer occurs in Oriental countries. Some of these differences may be artifactual and related to variability in reporting of prostatic cancer. Decreased overall life expectancy in some countries may also be contributory. Within the United States, prostatic cancer occurs most commonly in blacks.[5] Overall mortality is increased in blacks compared to white populations, and metastatic disease is evident more often at the time of presentation.

Some of the more interesting studies regarding the influence of race and

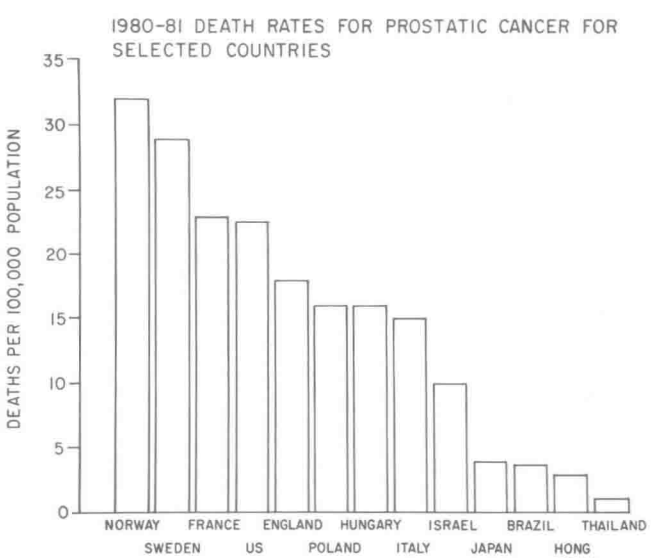

FIG 1–1.
Graph showing relative incidence of prostatic cancer for selected countries. Overall, clinically apparent prostatic cancer is most common in Scandinavian countries and least common in Oriental countries.

environment on prostatic cancer have involved populations of Japanese patients. Although the incidence of clinically apparent carcinoma of the prostate is relatively low in Japan and in first-generation Japanese migrants to the continental United States, the mortality from prostatic cancer rises in Japanese Americans living in the continental United States for more than one generation.[6] Similarly, the proliferative type of latent prostatic cancer is seen with increased frequency in Japanese migrants to Hawaii compared to those in Japan.[7] Thus, although race alone seems to be a factor influencing the frequency of prostatic cancer, these studies underscore the obvious additional impact of environmental factors.

Familial Factors

Carcinoma of the prostate occurs more frequently in the sons and siblings of patients who have developed clinically apparent disease (Table 1–1). A fourfold increase in the incidence of prostatic cancer occurs in the brothers of patients who develop the disease by the seventh decade of life.[8] Whether this indicates a genetic predisposition for prostatic cancer or is simply a reflection of exposure to similar environmental influences is uncertain. However, sons of patients with prostatic cancer have been found to have circulating serum testosterone levels that are somewhat lower than those of a control population with no family history of prostatic cancer.[8] The interpretation and significance of these studies is difficult to determine, but they do underscore the wisdom of a screening rectal examination and careful follow-up of male family members of patients with prostatic cancer.

Previous Prostatic Disease

A common concern among men with nonmalignant diseases of the prostate or genitourinary tract is the possible association between these problems and the subsequent development of carcinoma. The frequency of occurrence

TABLE 1–1.
Risk of Prostatic Cancer for Brothers of Patients With Known Prostatic Cancer*†

	AGE, YEAR						
	50–54	55–59	60–64	65–69	70–74	75–79	80–84
Cumulative risk of developing prostatic cancer							
Brothers	0.004	0.020	0.033	0.081	0.204	0.528	0.528
Control population (State of Utah)	0.001	0.005	0.012	0.029	0.054	0.089	0.132
Relative risk	4.0	4.0	2.75	2.79	3.78	5.93	4.0

*Modified from Meikle AW, Smith JA Jr, West DW: Familial factors affecting prostatic cancer risk and plasma sex steroid levels. *Prostate* 1985; 6:121–128. Used by permission.
†An overall fourfold increase in the probability of developing prostatic cancer is evident in brothers of patients with a known diagnosis of prostatic cancer compared with a general population of comparable age.

of prostatic cancer as well as benign prostatic diseases and the possible contribution of other factors make strong statements regarding possible associations difficult. However, there is no convincing evidence that a history of either bacterial or nonbacterial prostatitis or urethritis predisposes a patient to the development of carcinoma. Prostatic calculi are usually an incidental finding in patients with benign prostatic enlargement but have been reported in at least one study to occur with increased frequency in patients with prostatic cancer (Fig 1–2).[9]

There are conflicting data regarding the association of prostatic cancer and sexual practices. Some studies link sexual hyperactivity and promiscuity with an increased risk of prostatic cancer,[10,11] while others suggest increased risk for those with repressed sexual activity,[12] including Catholic priests.[13] Similar confusion is apparent in reviewing the data regarding dietary factors in the development of prostatic cancer. It has been suggested by some that a high-fat diet contributes to carcinogenesis within the prostate, but this is unproven. There is no apparent association between cigarette smoking or alcohol intake and the development of carcinoma of the prostate.

The age at which prostatic cancer increases in frequency correlates with the development of benign prostatic hyperplasia. Therefore, it has been speculated that there may be an association between the two events. Approximately 10% of patients undergoing a transurethral prostatectomy for presumed benign prostatic hyperplasia are found to have microscopic adenocarcinoma.

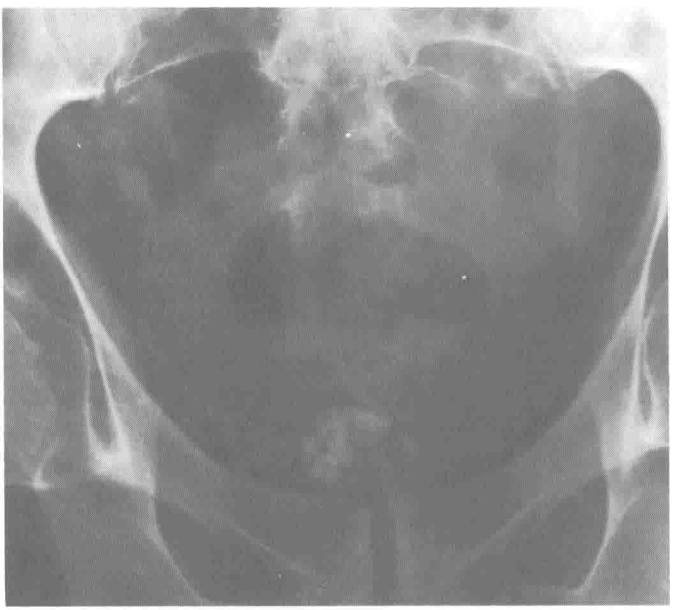

FIG 1–2.
Prostatic calculi visualized on plain film of pelvis. Prostate calculi are most commonly associated with benign prostatic hyperplasia rather than prostatic cancer.

However, the autopsy incidence of occult prostatic cancer in age-matched patients is similar. It seems likely that, despite the relatively common occurrence of prostatic cancer and benign enlargement in the same patient, etiologic factors for the two events are unrelated.

SYMPTOMS OF PROSTATIC CANCER

Knowledge of symptoms that may be associated with carcinoma of the prostate may help direct the clinician toward establishing the diagnosis and instituting appropriate therapy. Unfortunately, most localized prostatic cancers that are amenable to potentially curative therapy produce no symptoms. Locally advanced carcinoma of the prostate may cause symptoms of bladder outlet obstruction that mimic those seen in patients with benign prostatic hypertrophy. As the cancer enlarges, the flow of urine is restricted and patients may complain of hesitancy, dribbling, urinary frequency, nocturia, and a feeling of incomplete emptying. These symptoms may develop and progress more rapidly in patients with carcinoma of the prostate than in those with benign prostatic hyperplasia, but distinction between the two is not possible based simply upon symptoms and patient history. Sometimes, the voiding symptoms in patients with prostatic cancer are more related to rigidity within the prostatic capsule and bladder neck than to obstructive tissue alone. Hematuria, either gross or microscopic, may be seen occasionally in patients with prostatic cancer, but this is neither a sensitive nor a specific finding for the disease. Urinary tract infections may occur, especially if there is poor bladder emptying, but this also is a nonspecific finding. Independent of the effects of various treatments, there is generally no association between localized carcinoma of the prostate and sexual potency.

Patients with metastatic carcinoma of the prostate most often present with bone pain. Sometimes, especially in patients who have ignored bone pain or mistakenly attributed it to arthritis, a pathologic fracture or spinal cord compression is the presenting symptom. Cranial nerve palsies are seen occasionally in patients with basilar skull metastases. Lower-extremity edema may occur in situations where pelvic node metastases compromise venous return. Palpable lymph nodes, especially in the supraclavicular or inguinal region, may be the first sign of metastatic prostatic cancer. Soft-tissue metastases outside the lymphatic system are seen relatively frequently in patients with widespread skeletal metastases but are rarely the sole site of presentation of metastatic disease (Fig 1–3).

DIAGNOSIS OF PROSTATIC CANCER

Most often, the diagnosis of prostatic cancer is established because of a physical examination suggestive of the disease or signs and symptoms of metastatic tumor. The sensitivity and specificity of screening methods applied to the

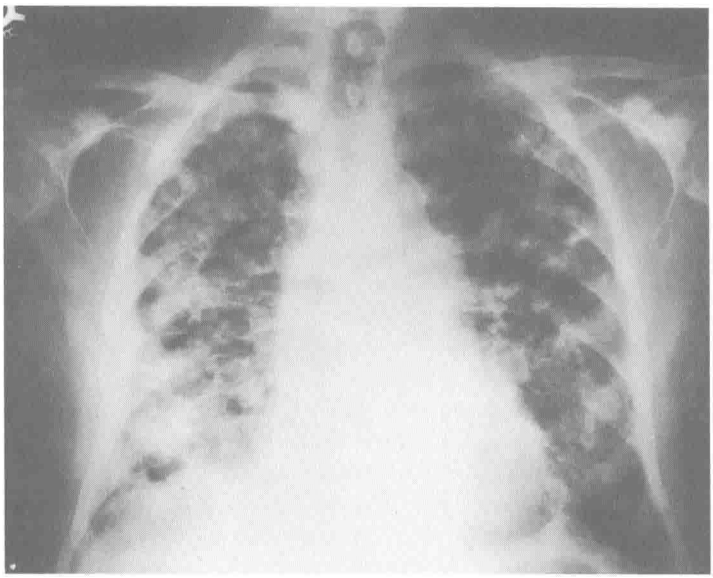

FIG 1–3.
Diffuse nodular and interstitial lung infiltrate from prostate cancer. Soft-tissue metastases of this extent are seen rarely without simultaneous bone involvement.

general population are insufficient for widespread application. Localized prostatic cancer is best detected by digital rectal examination, and it is recommended that this be performed on an annual basis in all men over the age of 50.

Prostatic Biopsy

Biopsy of the prostate is performed whenever there is a clinical suspicion of the presence of prostatic cancer. Usually, an area of induration, nodularity, or asymmetrical enlargement is detected on digital rectal examination. Sometimes, symptoms of distant metastatic disease have directed attention toward the prostate. In patients with metastatic adenocarcinoma of unknown primary, the prostate is sometimes considered as a source. However, in this setting, blind biopsy of a palpably normal prostate is unusually unrewarding.

By digital rectal palpation, a normal prostate gland is somewhat heart-shaped, with the base toward the bladder neck and the apex distally at the urogenital diaphragm (Fig 1–4). The base or superior aspect of the prostate is palpable as a transverse depression. Normal seminal vesicles are not palpable. The levator ani muscles are palpable at the lateral sulcus of the prostate. The normal consistency of the prostate is similar to that of the tip of the nose or the muscles of the thenar eminence of the hand; it is slightly compressible or spongy. Carcinoma of the prostate may be palpable as an area of nodularity that is raised from the surrounding surface of the prostate. Other times, the

nodularity is less apparent but there is a loss of the usual planes surrounding the prostate at the lateral sulcus or base. Some degree of induration is almost always palpable. Often, only a deep induration is detectable rather than any irregularity or nodularity of the prostate.

Although a rectal examination may identify patients in whom there is a suspicion of adenocarcinoma of the prostate, other causes of prostatic induration and nodularity exist. Nodular forms of benign prostatic hypertrophy can occur resulting in irregular prostatic growth. Usually, these nodules are less indurated than those found in patients with carcinoma. Prostatitis or prostatic calculi can result in abnormal prostatic induration. An unusual form of prostatitis, granulomatous prostatitis, may be extremely difficult to distinguish from carcinoma by digital examination (Fig 1–5). Finally, postoperative changes and fibrosis, especially after a previous transurethral prostatectomy, can produce nodularity and induration difficult to distinguish from carcinoma.

The accuracy of a digital rectal examination as a screening test for carcinoma of the prostate is dependent upon the experience of the examiner and the frequency with which biopsy is recommended. However, prostatic biopsy should be performed whenever there is a palpable abnormality of the prostate that is suspicious of carcinoma if the patient is considered to be a candidate for therapy once the diagnosis is established. In general, this implies that there are some patients in whom biopsy may be deferred or, perhaps, not performed at all despite a clinical suspicion of prostatic cancer. Some elderly patients or those with significant medical problems may not be considered candidates for curative therapy by either surgery or irradiation. In these cir-

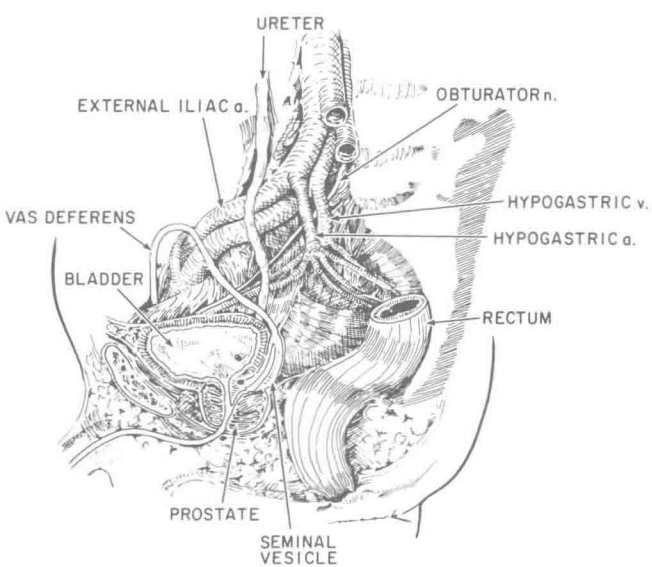

FIG 1–4.
Sagittal view of the pelvis showing the anatomical relationships of the prostate.

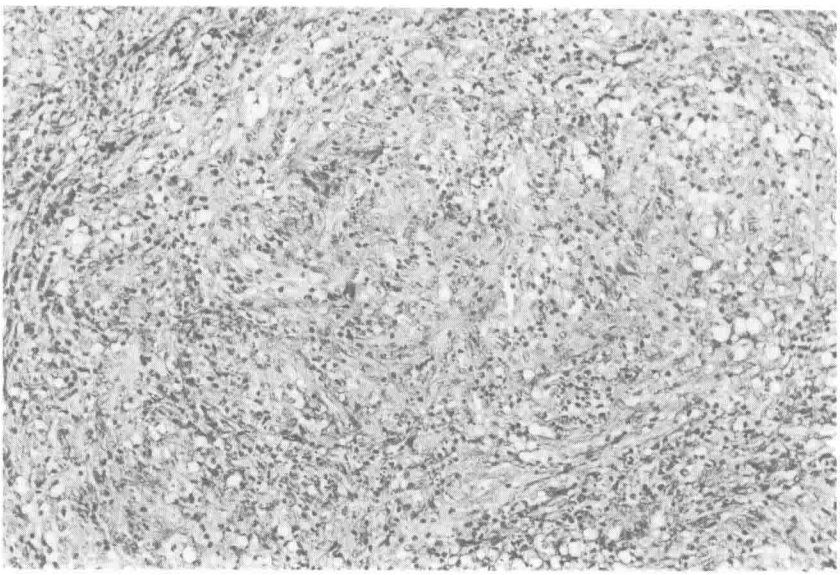

FIG 1–5.
Typical histologic findings of granulomatous prostatitis. Although the histologic changes are characteristic, physical examination may show an indurated lesion that cannot be distinguished from prostatic cancer.

cumstances, biopsy may be unnecessary and a needlessly invasive procedure if no immediate treatment is planned. The patient should be informed of the abnormality of the prostate and the possibility of carcinoma. If there is evidence of either local or distant disease progression, biopsy can be performed to confirm the diagnosis and appropriate palliative therapy instituted.

Once the decision has been made to perform a prostatic biopsy, a number of options are available. The decision regarding the type of biopsy should depend upon the experience and preference of the surgeon and pathologist as well as the size and location of the nodule.

Transperineal Biopsy

Core biopsies of the prostate can be obtained by placing a needle through the perineum into the suspicious area of the prostate (Fig 1–6). With a finger inserted into the rectum, the tip of the needle can be palpated and is directed into the suspicious area. Either a Vim-Silverman or a Tru-Cut needle is satisfactory for this purpose (Figs 1–7 and 1–8). The procedure can be performed with local infiltration of xylocaine into the perineum, but spinal or general anesthesia is often used.

Patients are placed in the lithotomy position. Often, prostate needle biopsy is preceded by cystoscopy for staging purposes (see chapter 2). An index finger is inserted into the rectum and the needle enters the perineum approxi-