PROSTATE CANCER is the most commonly diagnosed cancer in men and the second leading cause of cancer-related deaths. An estimated 186,320 new cases and 28,660 deaths from prostate cancer will occur in 2008. At the time of diagnosis, most patients have local or regional disease, with only about 5% having metastatic disease.

In this article, I’ll describe management of metastatic prostate cancer and how these interventions can help improve your patient’s quality of life. For more on prostate cancer risks and diagnosis, see Prostate cancer basics.

Assessment pointers
Start your assessment with a history, focusing on the patient’s urinary tract symptoms. Ask him to describe his usual voiding pattern, color and volume of urine, and symptoms that occur during voiding, such as dribbling. Ask about urinary frequency, nocturia, and hematuria. Because advanced prostate cancer commonly metastasizes to bones, ask him about back, hip, rib, or other bone pain. Unusual bleeding could also indicate bone marrow metastases.

Take a sexual history, which includes changes in sexual function and desire, sexual partner preference, ability to achieve and maintain an erection, penile discharge or lesions, scrotal pain or swelling, and history of sexually transmitted diseases. Perform medication reconciliation, watching for types of drugs (including cough and cold medications) that can affect the patient’s voiding pattern.

Document the patient’s vital signs and weight. Ask him about his usual weight and if he’s lost weight recently. Check his skin for ecchymoses and his legs for edema. (Unilateral lower extremity edema could be caused by deep vein thrombosis [DVT].) Bilateral edema may be related to lymph node metastases and lymphedema or bilateral DVTs. Assess his abdomen for masses and his suprapubic area for a distended bladder, using palpation and percussion to outline the bladder size. A physician or advanced practice nurse usually performs a digital rectal exam (DRE). The patient also should have gastrointestinal, cardiac, and pulmonary assessments.

Using hormonal therapy
Typically, prostate-specific antigen (PSA) levels fall to undetectable if all the cancer cells have been removed, for
example by radical prostatectomy. If the patient’s PSA level doubles in less than 10 months, he’s at risk for developing metastatic disease and may benefit from early hormonal therapy.  

Hormonal therapy, also known as androgen deprivation therapy (ADT), is the main form of treatment for metastatic disease. Initially, prostate cancer is sensitive to androgens such as testosterone, so removing testosterone and adrenally-produced androgens can reduce tumor size and PSA level. However, prostate cancer eventually becomes refractory to hormonal therapy. Even though hormonal therapy can cause hot flashes and sexual dysfunction, it’s often better tolerated than chemotherapy, and is continued for as long as it’s effective. Most patients continue on luteinizing hormone-releasing hormone (LHRH) therapy even after disease progression.

Initial hormonal therapy for androgen-sensitive disease includes either surgery (bilateral orchiectomy) or medical treatment with LHRH agonist therapy. These therapies are considered equivalent in efficacy.

- **Bilateral orchiectomy**, or surgical removal of the testes with or without replacement with prostheses, immediately reduces testosterone levels. The advantage of this option is that the patient won’t need to return periodically for injections of LHRH agonist therapy. However, the loss of testosterone leads to adverse reactions such as hot flashes, reduced libido, and impotence, and the surgery may raise psychosocial issues, including feelings of loss of masculinity.  

- **LHRH agonist therapy** initially causes a surge in testosterone before testosterone falls to very low levels and the tumor shrinks. In susceptible patients, the increase in testosterone may be associated with a temporary increase in tumor size (an event called a flare). Some patients can’t tolerate an increase in tumor size. For example, a patient with spinal metastases could develop spinal cord compression and paralysis. Adverse reactions to LHRH therapy include hot flashes, osteoporosis, dyslipidemia, muscle atrophy, cognitive dysfunction, gynecomastia, and anemia.

Antiandrogens may be given before or with LHRH agonist therapy to reduce the risk of tumor flare. The combination of an LHRH agonist and an antiandrogen is called maximal androgen blockade (MAB). Luteinizing hormone-releasing hormone agonists reduce testosterone levels by affecting the production of LHRH, but antiandrogens block testosterone effects on prostate cells, thereby preventing the hormones’ biological effects. Usually administered for 2 to 4 weeks before starting an LHRH agonist, antiandro-
gens can cause adverse reactions such as gynecomastia and breast tenderness. Because of the risk of hepatotoxicity, obtain liver function tests at baseline, after 1 month of therapy, and then every 3 months throughout therapy.

Education is crucial in helping your patient manage adverse reactions to hormone therapy. Teach him the importance of keeping appointments for obtaining PSA levels and receiving scheduled LHRH therapy injections. At each visit, assess him for adverse reactions to therapy.

Let’s look now at some ways that ongoing education can help him cope with his diagnosis and treatment.

**Bodily changes**
Therapy can increase your patient’s risk of osteoporosis, falls, and fractures. It also can change his metabolism, raising his risk of dyslipidemia and hyperglycemia. Obese patients have a greater risk of disease relapse after prostatectomy than patients of normal weight.5

Teach your patient to follow dietary and exercise guidelines to reduce weight and maintain muscle strength. He should eat a diet high in fiber; with lean meats and complex carbohydrates; and low in fat, cholesterol, and refined carbohydrates. His fasting glucose level should be measured after 1 year of ADT.6 Monitor his lipid profile results and teach him about lipid-lowering medications if prescribed.

Bone mineral density studies should be performed at baseline and as necessary. Unless he has bone metastases, he should perform muscle-strengthening exercises. Teach him to increase his intake of calcium (1,000 mg/day) and vitamin D (400 international units/day), and to avoid tobacco and excess alcohol consumption.7

Bisphosphonate therapy with zoledronic acid can reduce pain and the risk of skeletal complications (such as fractures) from bone metastases. Zoledronic acid is a commonly used bisphosphonate approved for patients with at least one site of bone metastasis from hormone-refractory prostate cancer.8 Serious adverse reactions to bisphosphonate therapy are renal impairment and osteonecrosis of the jaw. Your patient should tell his dentist that he’s on bisphosphonate therapy, and have a dental exam and preventive dentistry before starting therapy. To reduce the risk of osteonecrosis from dental procedures, tell him to get permission from his prescriber before visiting the dentist.

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**Prostate perspectives**
The prostate gland is found in the pelvis, under the bladder and in front of the rectum. Because of this anatomic location, a clinician can palpate the prostate gland via digital rectal exam, as illustrated at lower left. The urethra passes through the prostate gland, which is broader at its base than apex.
Managing adverse reactions
Tell your patient about these potential effects of hormone therapy and how to handle them:

- **Gynecomastia.** Increased breast tissue is a common adverse reaction to ADT, because of the increased level of estrogen. Prophylactic radiation therapy to the breast before antiandrogen therapy helps reduce the risk of gynecomastia. Tell the patient to notify his health care provider of breast enlargement. Treatment options include surgery and tamoxifen.

- **Altered sexuality.** Loss of libido and erectile dysfunction (ED) are common with hormone therapy. Take an open nonjudgmental approach and ask questions so that your patient can feel comfortable discussing these issues. Reassure him that many treatments are available for ED; refer him to a urologist or a urology advanced practice nurse as appropriate.

- **Hot flashes.** These frequent, common, and annoying episodes of sweating and flushing are caused by vasomotor instability, and may be persistent. Treatment options include antidepressants such as selective serotonin reuptake inhibitors, and medroxyprogesterone acetate. Advise the patient to wear lightweight clothing and avoid hot-flash triggers, such as hot beverages and a hot environment.

- **Anemia and fatigue.** Tell your patient to notify his health care provider if he develops signs and symptoms of anemia, such as increasing fatigue, tachycardia, and shortness of breath. Exercise, prioritizing activities, and pacing activities may help ease fatigue.

- **Falls.** Teach him to take precautions to reduce his risk of falls, such as removing throw rugs, and advise him to avoid contact sports. If he's taking the antiandrogen drug nilutamide, warn him that he may develop vision changes and alcohol intolerance.

- **Hepatotoxicity.** Monitor his liver function tests and tell him to notify his health care provider if he develops jaundice or dark urine.

- **Diarrhea.** Tell your patient to manage this adverse reaction with anti-diarrheal drugs as recommended by his health care provider, and by reducing dietary fiber. Encourage him to drink fluids and eat potassium-rich foods to replace the water and electrolytes lost in diarrhea. If he develops signs and symptoms of dehydration, years in some patients. Other antiandrogens may be tried until the patient demonstrates a loss of response.10

Refractory disease
Often after 2 years of ADT, prostate cancer becomes increasingly refractory to hormones.11 If antiandrogen withdrawal wasn't tried previously, it may be done once the cancer is hormone-refractory and progressive. A small number of patients respond to antiandrogen withdrawal.12 If MAB wasn't used for initial therapy, the patient's

Heavy-duty therapy
Maximal androgen blockade (MAB, also called combined androgen blockade or CAB) combines an LHRH agonist and an antiandrogen. This treatment may be used for patients with metastatic disease progressing on LHRH therapy alone. Once the cancer no longer responds to this drug combination, antiandrogen therapy is withdrawn and the patient monitored for antiandrogen withdrawal response. Up to a third of patients whose cancer is growing, despite MAB therapy, may have tumor regression when the antiandrogen is stopped. This antiandrogen withdrawal response may last 5 or more months, but can last as long as 2 years in some patients. Other antiandrogens may be tried until the patient demonstrates a loss of response.10
extremity edema or signs and symptoms such as polydipsia and vision changes. The practitioner may lower the dose of hydrocortisone. The patient’s blood glucose level should be checked; patients with hyperglycemia may need to monitor blood glucose levels at home.

Adverse reactions to ketoconazole include hepatotoxicity, nausea, vomiting, adrenal insufficiency, and rash. Monitor the patient’s liver function tests at baseline and monthly during therapy. Corticosteroids given alone are known to have a palliative effect on prostate cancer, reducing pain and improving the quality of life, so the patient may be prescribed prednisone as a single agent.

Chemotherapy

When hormonal therapy doesn’t work, chemotherapy may be used to slow cancer growth, reduce symptoms, and improve the patient’s quality of life. Many patients with prostate cancer are older and have other health problems, such as cardiac and pulmonary disease or cognitive dysfunction, that may interfere with the ability to safely administer chemotherapy.

Before discussing chemotherapy, the health care provider will measure the patient’s testosterone level to ensure that castrate serum testosterone levels are still present. Docetaxel plus prednisone is considered first-line chemotherapy. To reduce the risk of a hypersensitivity reaction to docetaxel, premedicate the patient with dexamethasone as ordered.

Adverse reactions to chemotherapy, which vary from patient to patient, include peripheral edema, neutropenia, reduced left ventricular ejection fraction, fatigue, hair loss, dyspnea, and gastrointestinal (GI) problems. Docetaxel may also cause hepatotoxicity with elevated liver function tests.

Optimal pain management is crucial, along with laxatives and stool softeners to manage opioid-induced constipation. Administer adjuvant medications as needed to improve pain control. Palliative treatments such as radiation therapy or radio-pharmaceuticals may be used for bone pain.

When teaching a patient to cope with chemotherapy, focus on these common problems.

- GI adverse reactions. Encourage an anorexic patient to try new foods and flavors to tempt his taste buds. If he’s nauseated, offer antiemetics and advise him to avoid odors that trigger nausea. Tell him to call his health care provider if nausea and vomiting don’t respond to antiemetic medication.

If he has diarrhea, he should take anti diarrheal medication, drink plenty of fluids, and eat a low-fiber lactose-free diet. He should call his health care provider if diarrhea is excessive or persistent or if his mouth feels dry, urine output decreases, or if he’s dizzy or light-headed.

- Neutropenia. Teach him the signs and symptoms of infection, including a temperature of 100.5°F (38°C) or greater, chills, diaphoresis, sore throat, diarrhea, and a new or newly productive cough. Tell him to immediately notify his health care provider if he develops a fever.

- Hair loss. A hat or wig can keep the head warm and reduce heat loss.

- Reduced left ventricular ejection fraction. Tell the patient to call his health care provider immediately if his legs or ankles swell, he has trouble breathing, or he has less energy for his usual activities.

Palliative care should be considered for patients with refractory disease or those who aren’t candidates for chemotherapy. Refer the patient and his family to a social worker and hospice nurse as appropriate.

Hope for the future

Recent research has improved the outcomes for men with prostate cancer. The disease is now usually diagnosed at an earlier stage, and treatments have improved. By understanding these developments, you can help educate and support your patient throughout diagnosis and treatment.

REFERENCES


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