82-Year-Old Man With Bilateral Leg Swelling

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An 82-year-old man with a medical history remarkable for chronic heart failure, diabetes mellitus, benign prostatic hyperplasia (BPH), and degenerative joint disease presented to the outpatient clinic with bilateral lower extremity swelling of 1 month’s duration. The lower extremity edema was bilateral but slightly worse on the right. The edema worsened during the day but transiently improved when the patient was in the supine position. He had no edema worsened during the day but transiently improved the patient was in the supine position. He had no symptoms of paroxysmal nocturnal dyspnea, angina, or orthopnea. He denied prolonged immobility and had no history of deep venous thrombosis (DVT). He had a history of myocardial infarction 20 years previously with resulting chronic heart failure. Of note, he had no known history of kidney or liver disease and had no remote or recent history of smoking. He denied a history of cancer or recent surgeries.

The patient’s medications included aspirin, atenolol, metformin, simvastatin, terazosin, and acetaminophen-oxycodone for arthritic hip pain. On examination, he was afebrile, with a blood pressure of 144/76 mm Hg and a regular pulse of 71 beats/min. He appeared in mild distress secondary to the hip pain. Bilateral 2+ pitting edema was noted up to 6 cm below each knee. The right calf was 3 cm larger than the left. He had evidence of chronic venous stasis changes in both lower extremities, and no collateral veins were present. No open ulcers or wounds were noted, and no cords were palpated. There was localized pain with palpation of the posterior aspect of the calf on the right. Findings on examination of the lungs and heart were normal. His jugular venous pressure was not elevated. Findings on neurologic, abdominal, and skin examinations were unremarkable, except as noted. Musculoskeletal examination showed tenderness to palpation of the lateral aspect of the left hip. No joint swelling, deformity, or erythema was present.

1. Which one of the following is a major criterion for the estimation of the pretest probability for DVT?
   a. Active cancer
d. Presence of DVT on lower extremity ultrasonography
   c. A positive Homan sign
   e. Venous stasis pigmented changes

   The Wells criteria or Wells scoring system for the detection of DVT consists of 9 distinct factors that help estimate the pretest probability for DVT.1,2 One point is given for the presence of each of the following: (1) active cancer, (2) immobilization of the lower extremities, (3) being bedridden or having undergone recent surgery, (4) swelling of the entire lower extremity, (5) calf swelling of greater than 3 cm in the symptomatic vs the asymptomatic extremity, (6) pitting edema confined to the symptomatic leg, (7) previously documented DVT, (8) localized tenderness along the distribution of the deep venous system, and (9) superficial, nonvaricose veins in the symptomatic extremity. Notably, the final criterion subtracts 2 points from the total if an alternative diagnosis is at least as likely as DVT. The pretest probability of DVT is high with a score of 3 or more, moderate with a score of 1 or 2, and low for scores of zero or less.1,2

   Leg erythema is not a criterion in the Wells scoring system. Homan sign, which is calf pain with dorsiflexion of the foot, was once a widely used test. However, newer evidence shows that only 15% of patients with a positive Homan sign have a DVT.3 Lower extremity ultrasonography to monitor for the presence of DVT is a diagnostic test typically done if the Wells score indicates a high probability for DVT but is not part of the scoring system itself.1,2 Venous stasis pigmented changes are associated with chronic venous insufficiency and not DVT.

   When calculating the Wells score for the patient in this case, 1 point was given for (1) entire leg swelling, (2) a right calf that was more than 3 cm larger than the left calf, and (3) localized tenderness with palpation in the distribution of the deep venous system. Pitting edema was present, but it was not isolated to the symptomatic leg, so no point was given. Because no other diagnosis was as likely as DVT, the final Wells score was 3, making his pretest probability of DVT high.

   Bilateral lower extremity ultrasonography showed no evidence of DVT. Additional laboratory testing yielded the following results (reference ranges provided parenthetically): a potassium level of 5.4 mmol/L (3.6-4.8 mmol/L), a sodium level of 140 mEq/L (135-145 mEq/L), and a creatinine level of 2.6 mg/dL (0.8-1.2 mg/dL). Records

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See end of article for correct answers to questions.

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from 1 year ago indicated that his baseline creatinine level was 1.2 to 1.3 mg/dL. For assessment of other etiologies of his lower extremity swelling, the patient underwent dobutamine stress echocardiography, which revealed a left ventricular ejection fraction that was unchanged from his baseline of 25% reported the year before, along with a right ventricular systolic pressure of 59 mm Hg (15-25 mm Hg), no ischemic changes, and no new regional wall motion abnormalities. Given the elevated creatinine level, a urinalysis and urine microscopy were performed and showed no organisms, red blood cells, or leukocytes that would suggest hematuria or infection. The protein-to-osmolality ratio did not suggest substantial proteinuria. Renal ultrasonography revealed bilateral hydronephrosis.

2. Which one of the following is the most likely cause of this patient’s bilateral hydronephrosis?
   a. Transitional cell carcinoma
   b. BPH
   c. Renal calculus
   d. Schistosoma haematobium infection
   e. Renal cell carcinoma

   Transitional cell carcinoma of the bladder is unlikely to be the cause of this patient’s bilateral hydronephrosis. He had experienced no weight loss or gross hematuria, which are commonly associated with transitional cell carcinoma. Tobacco and aniline dyes are often associated with bladder cancer, but this patient had no known exposure to these carcinogens.5

   This patient has a known diagnosis of BPH, which is very common among older men. Benign prostatic hyperplasia can cause outlet obstruction that can ultimately lead to bilateral hydronephrosis.3,4 A renal calculus is an unlikely cause of this patient’s hydronephrosis because of the lack of evidence of hematuria on urinalysis and urine microscopy, the absence of stones on ultrasonography, and the presentation of bilateral obstruction.

   Schistosoma haematobium infection is uncommon in the United States. It is associated with contaminated water supplies and is often seen in travelers or persons from areas in which this organism is endemic, such as the Middle East. Patients usually present with hematuria, and the diagnosis is made by observing the trematode’s eggs in the urine.5 The drug of choice for treatment is praziquantel. Renal cell carcinoma is an unlikely cause of this patient’s hydronephrosis given the lack of hematuria, weight loss, and obstructing mass.6 Typically, renal cell carcinoma would cause only unilateral hydronephrosis.

   The patient was admitted to the hospital for further treatment. A urinary catheter was placed, which drained 1.8 L of clear urine. A presumptive diagnosis of BPH causing bilateral hydronephrosis and acute renal failure was made.

3. Which one of the following is true regarding BPH?
   a. It increases the risk of prostatic adenocarcinoma
   b. It typically develops in the peripheral zone of the prostate
   c. It is caused by hypertrophy of the prostate cells
   d. Terazosin is considered first-line therapy
   e. Elevated prostate-specific antigen (PSA) is specific for its diagnosis

   No evidence suggests that BPH is associated with prostate cancer, and BPH is not considered to be a premalignant lesion that could potentially lead to prostate cancer. Benign prostatic hyperplasia results from the growth of prostate cells. This growth starts in the transitional zone of the prostate and not in the peripheral zone. It is stimulated by dihydrotestosterone (DHT), a derivative of testosterone that is 10 times more potent because it dissociates from its androgen receptor more slowly.3,6,7 Often, BPH is thought to stand for benign prostatic hypertrophy; however, this is a misnomer because the condition results from cell hyperplasia. It becomes symptomatic when it causes urinary outflow resistance from compression on the prostatic urethra. Ultimately, this obstruction leads to detrusor muscle dysfunction and irregular bladder contractions.4 Once this occurs, first-line treatment is usually with an α-1 antagonist, such as terazosin, which prevents contraction of the prostatic smooth muscle. Prostate-specific antigen is a glycoprotein that is expressed by both normal and neoplastic prostate tissue. It can be elevated for many conditions, including BPH, perineal trauma, prostate cancer, and prostatitis.8 Therefore, the PSA is not specific for BPH.

   During the hospitalization, the patient’s electrolytes were corrected and he was placed on a low-sodium diet given his heart failure. The lower extremity edema gradually improved. The urology service was consulted for recommendations on managing his BPH. They advised continuing his urinary catheterization and maximized his dose of terazosin. Gradually, his creatinine level decreased to 2.2 mg/dL. The patient was scheduled for a follow-up visit in the urology and internal medicine clinics and was discharged from the hospital.

   Three weeks later, the urologist completed a flexible cystoscopy, which showed severely obstructing trilobar prostatic hyperplasia. The retroflex view of the bladder neck showed substantial circumferential intravesical protrusion of the prostate. Urodynamic studies revealed an atomic bladder. Finasteride was added to the patient’s medical management. He was taught to initiate intermittent catheterization and to attempt to void between catheterizations. He was then told to follow up with the urology service in 6 months for an additional urodynamic study and discussion about surgical intervention on the prostate.
4. Which one of the following statements is true regarding finasteride?
   a. It is an α-receptor antagonist
   b. It can cause symptoms of orthostatic hypotension
   c. It decreases the PSA level
   d. It usually reduces symptoms within 7 to 10 days of starting therapy
   e. It is a cause of priapism

   Finasteride has no α-blockade capabilities and does not induce orthostatic hypotension; however, α-1 antagonists used to treat BPH can produce symptoms of orthostasis. Finasteride is a 5-α reductase inhibitor that prevents the conversion of testosterone to DHT. A hormone that is much more potent than testosterone, DHT acts on the stromal and epithelial cells in the transitional zone of the prostate and induces these cells to replicate, resulting in prostatic hyperplasia and subsequent compression of the prostatic urethra. This urethral compression causes the symptoms associated with BPH. Finasteride has been shown to inhibit hyperplasia of the cells of the prostate, reduce urethral compression, and improve the symptoms of BPH.

   Notably, finasteride can produce a 50% or greater decrease in serum PSA levels during the first 3 months of therapy, and this decrease persists as long as treatment with the drug is continued. This decrease is most likely secondary to the direct interference by finasteride with the prostatic intracellular androgen response mechanism. Finasteride has not been associated with priapism but has been associated with erectile dysfunction and decreased libido.

   On the same day as his urology visit, the patient also had a follow-up visit in the internal medicine clinic. His creatinine level was found to have decreased further to 1.5 mg/dL. He stated that he “felt better than he had in months.” Physical examination revealed substantially reduced bilateral lower extremity edema and a complete resolution of his hip tenderness. He inquired about alternative therapies that may be used to treat his BPH.

5. Which one of the following alternative therapies has been shown to be effective for symptom reduction in BPH?
   a. Echinacea
   b. Saw palmetto
   c. Ginseng
   d. Garlic
   e. St John’s wort

   Evidence for the treatment of upper respiratory tract infections with echinacea, an herbal product, is inconclusive. Extracts of the fruit from saw palmetto have been used for its effects on BPH. The exact mechanism of action is unclear, but it is hypothesized that saw palmetto produces an antiandrogen effect, relaxation of the lower urinary tract smooth muscle, and antimuscarinic effects. Randomized trials and meta-analyses have shown that saw palmetto has improved objective measurements and symptoms in patients with BPH.

   Ginseng is a perennial plant that is predominantly used for sexual dysfunction, diabetes, and mental performance. Studies have indicated that garlic is likely effective for the treatment of claudication and hypercholesterolemia. St John’s wort is derived from the Hypericum perforatum plant and is most commonly used for the treatment of depression.

   Given the improvement in the patient’s urologic symptoms and initiation of finasteride, no alternative therapy was begun. The patient is awaiting 6-month follow-up and is currently doing well.

DISCUSSION

Benign prostatic hyperplasia is a common medical condition that affects men as they age. It results from the actions of DHT, which is converted from testosterone by the enzyme 5-α reductase. Dihydrotestosterone is much more potent than testosterone and acts on cells in the transitional zone of the prostate, leading to prostatic hyperplasia and compression of the prostatic portion of the urethra. This in turn produces the symptoms of BPH, which include urinary hesitancy, decreased urinary stream, a sensation of incomplete voiding, and nocturia. The prevalence of BPH increases with age. In fact, BPH affects nearly 80% of men older than 70 years.

The diagnosis of BPH requires the combination of a thorough medical history, physical examination findings, and results of laboratory tests (eg, urinalysis, PSA screening test). None of these factors alone can be used to diagnose BPH definitively. The American Urological Association Symptom Score is an objective measurement of symptoms associated with BPH and aids in its diagnosis.

The treatment of BPH varies and can range from observation to medical and surgical therapy. Treatment is based on symptom severity. Patients with mild symptoms can be monitored at regular intervals. They should be counseled to limit their evening fluid intake and avoid caffeine. In patients with moderate to severe symptoms, more aggressive management is indicated. The medication armamentarium for the treatment of BPH includes α-1 antagonists and 5-α reductase inhibitors. First-line therapy is usually α-1 antagonists, such as tamsulosin or terazosin. Finasteride and dutasteride, which are 5-α reductase inhibitors, can be added to or replace α-1 antagonists. Surgical interventions are also available under the guidance of a urologist.
Indications for urologic referral include moderate to severe symptoms despite medical therapy, recurrent urinary tract infections, persistent gross hematuria, urinary retention, bladder stones, and obstructive kidney disease. Saw palmetto, an herbal medication, has been successfully used to treat the symptoms of BPH.\textsuperscript{1,12}

REFERENCES


