UNIT NO. 5

DISEASES OF THE PROSTATE

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INTRODUCTION

"Nothing in life is to be feared. It is only to be understood."
Marie Curie

An aura of mystery and fear, tinged with a dose of false beliefs and blissful ignorance, often accompany the afflictions of the prostate. We looked at three common but often misunderstood conditions that affect thousands of men everyday, and present an overview of the current treatment modalities available.

BENIGN PROSTATIC HYPERPLASIA (BPH)

It is estimated that from the age of 40 onwards, the incidence of BPH increases from an average of 23% to 88% by the age of 80 on histological examination. However, not all patients with histological evidence of BPH require treatment. Symptoms of BPH rarely presents before 60 years of age.

Clinical Presentation

The most common clinical presentation of patients requiring surgical treatment is acute retention of urine. Other symptoms of bladder outlet obstruction include hesitancy, poor stream and intermittency. Irritative symptoms of nocturia, frequency and urgency may supervene. Less common symptoms include painless gross haematuria, recurrent urinary infection, and chronic retention of urine resulting in uraemia and overflow incontinence. Many younger patients with urinary symptoms as a result of fluid imbalance or anxiety disorders. A voiding diary often demonstrates the increased total urine output and normal functional storage capacity. The important differential diagnoses are carcinoma of the prostate, and the various types of neurogenic bladders especially diabetes mellitus and Parkinson's disease. In the elderly bed-ridden patients, it is important to exclude chronic constipation with impacted stool as a cause.

In the physical examination, a non-tender palpable bladder after micturition would indicate chronic retention of urine. Digital rectal examination demonstrating a smooth, globular and firm prostate would indicate BPH, whereas an irregular and hard prostate would suggest malignancy.

Investigations

At the initial screening, urine dipstix is helpful in detecting haematuria, pyuria and glycosuria, and a serum PSA level allows screening for prostate cancer. Further testing may be warranted if initial tests are abnormal.

Urine is sent for culture and sensitivity for those patients with UTI. In patients with retention of urine, a KUB x-ray should be done to exclude bladder stone which is present in about 10% locally. Ultrasound of the kidneys, bladder and prostate has replaced IVU in assessing the patients for persistently high post-void residual urine, a large prostatic volume, prominent intravesical protrusion of the prostate and hydronephrosis. Uroflowmetry objectively tests for bladder outlet obstruction. A flow rate of less than 15 mls per sec with a voided volume of at least 150 mls indicates mild obstruction, and less than 10 mls per sec indicates significant obstruction. Post-void residual urine volume of more than 100 ml also suggests significant obstruction. A full urodynamic study with cystometrogram is indicated for patients with bothersome symptoms but a good flow rate. Flexible cystoscopy is only used for assessing patients suspected to have bladder neck stenosis, and those with previous transurethral surgery.

Treatment

BPH may be treated by watchful waiting, pharmacotherapy or surgery (Table 1). Patients with no bothersome symptoms and no significant obstruction can generally be managed conservatively and reassessed 6-monthly. For those with significant obstruction, surgery would be advised. Surgery is also indicated for those with acute retention of urine and failed trial-off catheter, and for those complicated by chronic retention, bladder stone, recurrent urinary tract infections or recurrent gross haematuria. The procedure of choice is transurethral resection of prostate (TURP). Open prostatectomy is seldom indicated. For the elderly patient, as long as he is ambulant, he would benefit from TURP.

Table 1. Management of benign prostatic hyperplasia

Severity	Remarks	Treatment
Mild	• No bothersome symptoms • No significant obstruction	Watchful waiting
Moderate	• Bothersome symptoms • Mild to moderate obstruction on uroflowmetry and transabdominal ultrasonography	Pharmacotherapy Surgery for failed medical treatment
Severe	• Severe obstruction on uroflowmetry and transabdominal ultrasonography, even if patient has no bothersome symptoms • Presence of complications such as repeated retention, bladder stone, recurrent urinary tract infections or recurrent gross haematuria	Surgery

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Pharmacotherapy

After excluding serious conditions such as prostate cancer, infection and azotemia, patients with symptoms affecting their daily routine, with mild to moderate obstruction, may be offered a trial of pharmacotherapy. Pharmacotherapy may be grouped into 3 categories: 1. alpha adrenergic blockers eg. Prazosin (Minipress), Terazosin (Hytrin), Alfusozin (Xatral) & Doxazosin (Cardura), 2. 5-alpha reductase inhibitors eg. Finasteride (Proscar) and 3. plant extracts eg. Permixon.

Alpha adrenergic blockers have been shown to be effective in improving symptoms. Side effects include dizziness, orthostatic hypotension. Patients on antihypertension medication will require titration of their antihypertension dosages. Because of the blood pressure lowering effect, its use in patients with coronary artery disease or cerebrovascular accidents is cautioned, although newer uro-selective blockers have been promoted as being safe for these patients. 5-alpha reductase inhibitors provide relief of symptoms and obstruction as well as prevention of progression of prostatic enlargement and acute retention of urine have been demonstrated with the use of finasteride. At least 3 months usage is necessary before relief is to be expected and continued lifelong usage is required to maintain effect. Side effects include diminished libido, reduced ejaculation and impotence. It can, however restore hair growth. A PSA level should be taken prior to starting therapy as finasteride lowers serum PSA which may mask cancer development. Plant extracts are a mixed bag of compounds comprising different ingredients from various plant sources. Their mechanisms of action are not entirely clear and short-term randomized trials suggest some efficacy for certain preparations but proper studies with long term follow-up is lacking.

Surgery

Currently TURP is still the gold standard in the treatment of BPH with significant obstruction. Post-operatively, the patient is kept on continuous bladder washout for 24 hours and sent home a day after the removal of catheter on the 3rd post-operative day. Post-operative pain is minimum and they can resume their meals the same evening. They can return to normal activity two weeks after discharge from hospital.

The mortality is less than 1% and morbidity is minimum. Less than 10% of patients require blood transfusion. About 5% of patients may have difficulty in urinary control due to urgency and temporary stress incontinence. Less than 1% would have total incontinence. The majority (60%) would have the side effect of retrograde ejaculation and should be warned about this. They should be reassured that this side effect will not affect their health though some may find it less pleasurable at orgasm. Possibility of impotence is low, less than 4%. After discharge from hospital, most patients would still complain of irritative urinary symptoms which should improve within a few weeks. About 16% of patients have urinary tract infection and could be improved with antibiotics. Secondary haemorrhage (about 7%) can occur up to 4 weeks after surgery; and if severe, would need readmission for further management with bladder washout and possible cystodiathermy. Patients should be encouraged to keep their bowel movements regular with laxatives if necessary and have high fluid intake. Urethral strictures and bladder neck stenosis (5%) may occur with a typical history of good stream immediately after surgery with gradual deterioration subsequently after a few months to a few years. The chance of recurrent adenoma causing symptoms requiring re-TURP is about 10% in 10 years.

Indications for Referral to the Urologist

1. Persistent bothersome symptoms
2. Presence of gross haematuria and incontinence
3. Hard and/or irregular prostate
4. Palpable bladder and/or high residual urine
5. PSA ≤ 4 ng/mL
6. Proven UTI.

PROSTATITIS

Prostatitis is one of the most over-diagnosed conditions in urology. Essentially it is a diagnosis of exclusion. While acute bacterial prostatitis presents in a classical, dramatic fashion, there is no generally accepted, clearly defined criteria for chronic prostatitis. It is important to note that every bacteriologically proven urinary infection in man should be investigated. Unlike sexually active females who experience lower urinary tract infection fairly frequently, men suffer urinary infection generally as a result of some predisposing pathology.

Classification

The traditional classification based on Meares-Stamey's four-glass test has been largely abandoned. To improve the diagnosis and management of prostatitis, the National Institutes of Health (NIH) established an International Prostatitis Collaborative Network. The 1998 consensus conference from this network classified prostatitis syndromes into 4 categories (Table 2). A diagnostic algorithm helps to identify important treatable conditions in the initial office evaluation of prostatitis-like symptoms such as chronic pelvic pains, perineal pain and dysuria (Table 3).

Table 2. Definition and classification of prostatitis

Class	Subtype	Remarks
I	Acute bacterial prostatitis	Acute infection of the prostate with positive laboratory findings: positive urinalysis or urine culture, leukocytosis
II	Chronic bacterial prostatitis	Recurrent infection of the prostate
III	Chronic prostatitis/chronic pelvic pain syndrome	No demonstrable infection found.
A	Inflammatory	Leukocytes found on expressed prostatic secretions, urine after prostatic massage, or semen
B	Non-inflammatory	No evidence of inflammation found on expressed prostatic secretions, urine after prostatic massage, or semen
IV	Asymptomatic inflammatory prostatitis	Absence of subjective symptoms, but white blood cells found in prostatic secretions, or in prostate tissue during an evaluation for other disorders

Acute bacterial prostatitis

About 5% of prostatitis syndromes have bacterial prostatitis. These patients present with classical symptoms of an acute urinary tract infection, including urinary frequency, dysuria, perineal and low back pain. Some of them may have constitutional symptoms such as fever, malaise, and myalgia. Digital rectal examination reveals a tender, boggy prostate. Polymorpholeukocytosis is usually present and urinalysis and culture typically reveal bacteriuria and pyuria caused by well-recognised uropathogens, especially *Escherichia coli, Klebsiella, Proteus mirabilis, Enterobacter, and Staphylococcus aureus*. Treatment entails bed rest, antipyretics, analgesics, hydration and antibiotics (trimethoprim-sulfamethoxazole or fluoroquinolones) for 3–4 weeks. Acutely ill patients may need admission for broad-spectrum parenteral antibiotics such as ceftriaxone. Chronic prostatitis and prostatic abscess may follow unresolved acute prostatitis, especially in diabetics. Small prostatic abscesses are treated with long-term antibiotics and larger ones are drained by surgery via the transurethral route.

Chronic bacterial prostatitis

These patients present with recurrent intermittent episodes of bacterial urinary tract infections with similar symptoms as acute prostatitis, but with a more insidious onset. Clinical examination is often unremarkable. A prior documentation of bacterial prostatitis is helpful in diagnosis. Classically, expressed prostatic secretions and urine obtained after prostatic massage show bacterial colony counts that are at least 10-folds higher than bladder urine samples. Antibiotics which are lipid soluble to penetrate the prostatic lipid membrane (trimethoprim-sulfamethoxazole or fluoroquinolones) are used and are curative after 4–6 weeks in 33–50% of patients. Treatment may even be extended up to 12 weeks in selected patients.

Chronic prostatitis/chronic pelvic pain syndrome (CPPS)

More than 90% of symptomatic patients have chronic abacterial prostatitis or CPPS. The primary feature of these patients is urological pain and they must have had prior assessment to exclude presence of active urethritis, urogenital cancer, urinary tract disease such as BPH, functionally significant urerthral stricture, or neurological disease affecting the bladder. Patients with the inflammatory subtype have leukocytes in their expressed prostatic secretion, post-prostate massage urine or semen. In contrast, patients with the non-inflammatory subtype have no evidence of inflammation. There exists a wide range of treatment modalities, many of which may offer limited improvement. Treatment includes NSAID, alpha blockers, 5-alpha-reductase inhibitors, muscle relaxants, hot sitz bath, repeated prostatic massage and microwave thermotherapy. The role of empirical antibiotics is unclear and the potential benefit needs to be balanced against the cost and side effects. Surgery is not indicated in the treatment of most chronic prostatitis syndromes unless a specific indication is discovered during patient assessment.

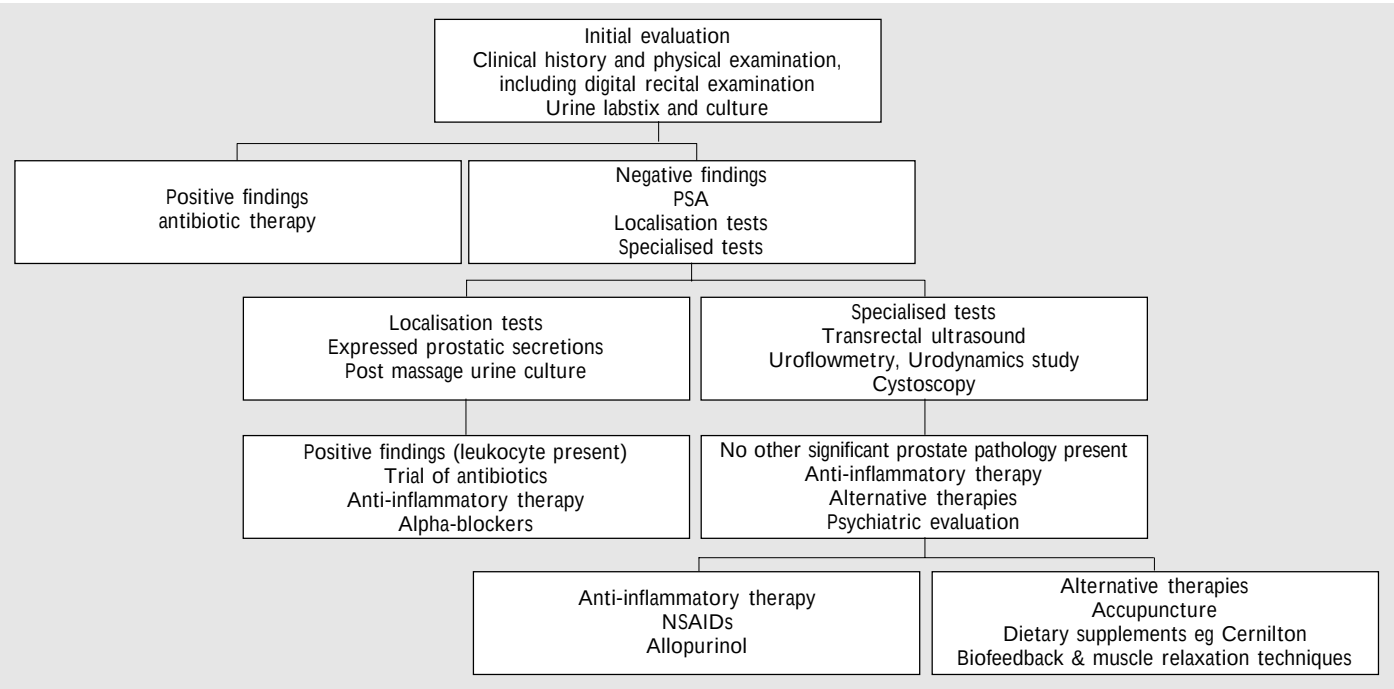
Asymptomatic inflammatory prostatitis

These patients are usually diagnosed during evaluation for other genitourinary tract issues and have no history of genitourinary tract pain. These evaluations may include transrectal ultrasound-guided biopsy for raised PSA level.

Prostate Cancer

Prostate cancer has risen to be the sixth most common cancer in Singapore men. It is rare below the age of 50 and is most common between the ages of 70 to 80 years. It is often diagnosed late because it arises from the posterior aspect of

Table 3. Diagnostic algorithm for prostatitis-like symptoms



the gland and by the time it involves the urethra anteriorly to give rise to symptoms of urinary obstruction it has already spread outside the prostate gland, often to the bone.

Diagnosis

With the wide spread use of prostate specific antigen (PSA) since the early 1990s in Singapore, and routine digital rectal examination (DRE), prostate cancer is now being diagnosed much earlier, before it spreads. The normal value of PSA is 0 to 4.0 ng/ml; above 20 ng/ml there is 70% chance of cancer, while with a value between 4 to 20 ng/ml, the risk is roughly 20–30%, many patients (about 70%) have benign prostatic hyperplasia or prostatitis. Transrectal ultrasound and biopsy need to be done to differentiate the various types of prostatic diseases.

Prostate cancer is staged by the extent of involvement of adjacent structures and its histological grading. Organ-confined cancer (T1-2) does not extend beyond the prostatic capsule whereas extra-capsular disease (T3-4) can include the seminal vesicles, lateral pelvic wall or rectum. Lymph node involvement is determined by histological evidence of cancer cells and metastasis is confirmed by hot spots on T^{99} Technetium bone scan or x-ray evidence of metastatic lesions. Histological grade is classified by a Gleason score where a higher score denotes poorer cellular differentiation.

Treatment

For early localised disease (T1-2), the current accepted treatment is radical prostatectomy for those who are medically fit and have a life expectancy of 10 years or more. Radical radiotherapy is also an acceptable alternative. There may be a place for watchful waiting for those with incidental well-differentiated cancer.

For patients with extracapsular (T3-4) and metastatic disease, many of them also have significant degree of bladder outlet obstruction. The treatment of choice then would be transurethral resection of the prostate and bilateral orchidectomy (as hormonal treatment). For those with no obstruction or not keen for orchidectomy, hormonal treatment with stilbesterol, anti-androgens such as cyproterone acetate(Androcur), Flutamide or LHRH analogues (Goserelin, Lucrin) could be given to control the disease.

For patients with metastatic disease, the focus is on minimizing morbidity from skeletal events such as pathological fractures and vertebral compression fractures. Radiotherapy and operative management of the fractures may help to reduce immobility and control bone pain. Physicians managing these patients also need to look out for metabolic abnormalities such as hypercalcaemia which may be treated with intravenous saline hydration and concomittant diuretics. Hormonal therapy by orchidectomy or medical treatment can prolong symptom-free survival and delay onset of hormone-refractory prostate cancer.

Prognosis

For early disease with treatment, the 10 year survival rate is about 70%; while for patients with distant spread, the outlook is not immediately hopeless, the mean survival is still about 30 months and a number of them died *with* and *not* of their disease.

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LEARNING POINTS

- Symptoms of BPH rarely presents before 60 years of age
- The important differential diagnoses of BPH are carcinoma of the prostate, the various types of neurogenic bladders (especially diabetes mellitus) and Parkinson's disease
- After excluding serious conditions such as prostate cancer, infection and azotemia, patients with symptoms affecting their daily routine, with mild to moderate obstruction, may be offered a trial of pharmacotherapy
- Currently TURP is still the gold standard in the treatment of BPH with significant obstruction
- Prostatitis is one of the most over-diagnosed conditions in urology. Essentially it is a diagnosis of exclusion
- About 5% of prostatitis syndromes have bacterial prostatitis.
- More than 90% of symptomatic patients have chronic abacterial prostatitis or Chronic Prostatic Pain Syndrome
- Prostate cancer has risen to be the sixth most common cancer in Singapore men. It is rare below the age of 50 and is most common between the ages of 70 to 80 years
- The normal value of PSA is 0 to 4.0 ng/ml; above 20 ng/ml there is 70% chance of cancer, while with a value between 4 to 20 ng/ml, the risk is roughly 20-30%, many patients (about 70%) have benign prostatic hyperplasia or prostatitis.