Prostatitis

RNT Thin

Prostatitis, especially chronic prostatitis, is sometimes regarded as an obscure, ill-defined condition, perhaps because the anatomical location of the gland and ill-defined symptoms make diagnosis difficult. Treatment may appear time consuming and tiresome for doctor and patient, but by following established principles, diagnosis is often simple and management straightforward.

In recent years our understanding of prostatitis has improved, although its prevalence is unclear. In the UK and Holland, GPs diagnose prostatitis in 1–10 patients a year, while 3 months after treatment of urethritis, prostatitis is reported in 14–35% of patients (Thin, 1997a). This article addresses the pathogenesis, classification, symptoms, diagnosis and management of the common forms of prostatitis, with emphasis on chronic prostatitis. Chronic prostatitis is more common and more difficult to understand than acute prostatitis, a condition which is rarely seen in the Western world.

ANATOMY AND PATHOGENESIS

The prostate is a tuboalveolar gland with a fibromuscular stroma and four zones within a fibrous capsule. In young men the peripheral zone is the largest and, along with the central zone, comprises the bulk of the gland; between them is a narrow transitional zone and a thin periurethral zone (McNeal, 1989).

Histological examination shows inflammation to be peripheral and multifocal. Infection may be related to the right angle at which the ducts enter the urethra compared with the oblique angle of entry of the ducts draining the central zone (Thin, 1997a). Urinary reflux into the prostate may be responsible for infection (Kirby et al, 1982), while prostatic calculi may be infected (Eykyn et al, 1974). Recent ultrasound reports of calcification in the area around the urethra also suggest that inflammation may be more central and related to intraprostatic reflux (D Rickards, 1999, personal communication).

The cause of the symptoms of prostatodynia (see below) are unclear. They may be related to tension myalgia of the pelvic floor muscles, outflow problems or referred pain. Emotional and psychiatric conditions may also be present (Berguis et al, 1996).

CLASSIFICATION

Prostatitis is classified as acute and chronic (Drach et al, 1978). The lower urinary tract quantitative localization procedure (Meares and Stamey, 1968), allows subdivision of chronic prostatitis into chronic bacterial prostatitis (CBP), chronic non-bacterial prostatitis (CNBP) and prostatodynia (Drach et al, 1978). In CBP a urinary pathogen is isolated from the expressed prostatic secretion (EPS). In CNBP inflammation is shown by increased numbers of white cells in the EPS but no organism can be identified. In prostatodynia there are symptoms of chronic prostatitis but neither organisms nor an excess of white cells are found (Drach et al, 1978).

SYMPTOMS

In acute prostatitis there are marked urinary symptoms with frequency, dysuria, and urgency, symptoms of prostatitis such as perineal pain, low backache and penile pain, and febrile symptoms including arthralgia and myalgia (Meares, 1987).

In chronic prostatitis there may be perineal ache, lower abdominal or suprapubic pain, penile pain especially at the tip, testicular pain, discomfort or pain on ejaculation, and rectal pain; urinary symptoms such as dysuria and frequency are much less prominent than in acute prostatitis. The first five of these symptoms may be more discriminatory than the remainder (Neal and Moon, 1994; Krieger et al, 1996a).

Dr RNT Thin is Senior Physician in the Department of Genitourinary Medicine, Guy's and St Thomas' Hospital Trust, London SE1 7EH

DIAGNOSIS

Acute prostatitis

This presents acutely with the symptoms outlined above. On rectal examination the prostate is extremely tender, often swollen, tense and warm. There is fever and tachycardia. Urine culture shows a pathogen such as *Escherichia coli*, *Proteus*, *Klebsiella* or *Pseudomonas* spp., enterococci, *Staphylococcus aureus*, or less commonly anaerobes such as *Prevotella* spp. or anaerobic streptococci. Blood culture may also be positive for the same organism. Prostatic massage should not be undertaken as it will be extremely painful, may precipitate bacteraemia and is of no diagnostic benefit as pathogens are readily isolated from the urine or blood (Meares, 1987).

The key to diagnosis is digital examination of the prostate. It should be remembered that acute prostatitis may be complicated by prostatic abscess or be secondary to bacteraemia, with a focus of infection elsewhere.

Chronic prostatitis

This is usually subacute in onset. It may present with the symptoms outlined or may be asymptomatic in patients with a history of recurrent urethritis or bacteruria. Digital examination may be normal, indicate localized tenderness, or mild general tenderness that is difficult to interpret. Diagnosis rests on the results of investigations.

The gold standard for diagnosing chronic prostatitis is the lower urinary tract localization procedure (Meares and Stamey, 1968). Although a little time consuming, and requiring close liaison with a microbiological laboratory, this will reliably provide a basis for diagnosing and differentiating CBP, CNBP and prostatodynia.

Diagnosis relies on prostatic massage of the non-tender prostate and analysis of EPS by microscopy and culture. Pre-existing urethritis or bacteriuria should first be treated with a non-prostate penetrating antimicrobial. Ejaculation should be avoided for 2 days before the procedure is undertaken, and urine should be held for at least 2 hours beforehand.

The procedure: The prepuce is fully retracted and the glans cleaned with saline. The first 5–10 ml of urine is collected (voided bladder urine 1; VB1). The patient then passes 100–200 ml urine, and a 5–10 ml sample of midstream bladder urine is collected (VB2). The prostate is then firmly massaged provided no tenderness is elicited; this involves passing the index finger down one lateral margin of the gland from top to bottom. This is repeated with the finger gradually moving toward the midline.

The median groove is then massaged from top to bottom. This procedure is repeated on the other side of the gland. The finger is then placed at the top of one side of the gland and passed downward and inward to the midline, gradually working down to cover one lobe. The median groove is massaged from top to bottom and the procedure repeated over the other lobe. Throughout the procedure a sterile receptacle such as a universal container is held under the meatus to catch the EPS.

Prostatic massage can be undertaken with the patient in the knee elbow position on a couch, or standing flexed from the hips with the elbows resting on a couch. Immediately after the EPS is obtained another 5–10 ml first catch sample of urine should be obtained (VB3), and the patient can then empty his bladder. As soon as possible a sample of EPS should be examined as a wet preparation under the microscope or using a white cell counting chamber to assess the number of white cells, to note whether they are clumped and the presence of oval fat bodies (macrophages containing fat droplets). The urine samples should be sent to the laboratory as soon as possible for microscopy and quantitative culture. The EPS should also be examined by quantitative culture. If an EPS sample is not obtained the VB3 sample should still be collected.

White cells and organisms in the VB1 alone, with normal findings in all other samples, indicate urethritis. White cells and organisms in the VB1, 2 and 3, with a normal EPS, indicate bacteriuria. White cells and organisms in the EPS and VB3, with a normal VB1 and VB2, indicate prostatitis. To diagnose CBP the number of organisms in the EPS and/or VB3 should be at least ten times that in the VB1 and 2. In CNBP ten or more white cells per x40 high power field, or 1000 white cells per mm^3, should be found in the EPS; the presence of clumps of five or more white cells, oval fat bodies and a pH of 8 are contributory evidence but are not in themselves diagnostic of prostatitis. In the absence of EPS, cells and organisms in the VB3 may indicate prostatitis.

Nickel (1997) suggested simply comparing pre- and postmassage urine samples, but Thin (1997b) indicated that examination of the EPS was more sensitive.

Transrectal ultrasound (TRUS), if available, should be performed before prostatic massage. This may show features of prostatitis and occasionally cysts or abscesses, which may symp-

tomically mimic prostatitis and respond to needle aspiration. TRUS will also help to exclude other conditions (Noble and Rickards, 1995).

Prostate-specific antigen should be requested, especially in men over 45 years of age. This may be elevated in prostatitis but reverts to normal with treatment. Elevation may also be because of benign prostatic hypertrophy or carcinoma.

DIFFERENTIAL DIAGNOSIS

Chronic prostatitis may rarely be caused by other organisms. Opinions vary as to whether *Chlamydia trachomatis* may cause chronic prostatitis. Doble and Taylor Robinson (1994) could not find evidence of *Chlamydia* but others using DNA amplification suggest this organism has a causative role (Krieger et al, 1996b). *Trichomonas vaginalis* and *Ureaplasma urealyticum* have been implicated in a few cases (Thin, 1997b). *Mycobacterium tuberculosis* must be remembered in areas of high prevalence and in the immunosuppressed, while *Neisseria gonorrhoeae* is rarely isolated.

Other unusual types of chronic prostatitis are parasitic, mycotic, and eosinophilic and non-eosinophilic granulomatous prostatitis (Meares, 1987). Chronic prostatitis may complicate and mimic bacteruria, calculi, abscesses, benign prostatic hypertrophy, outflow obstruction and, most importantly, carcinoma.

MANAGEMENT

Acute prostatitis

This is a serious condition so antimicrobial therapy should be started as soon as the clinical diagnosis is made and urine and blood samples taken for culture and sensitivities. Intense hyperaemia ensures good antimicrobial penetration throughout the gland. If there is any suggestion of bacteraemia, start with an intravenous drug effective against urinary tract pathogens, such as cefuroxime or cefotaxime. Once the patient is improving change to oral therapy.

In less severely ill patients, give oral therapy from the outset, such as ciprofloxacin 500 mg twice daily or ofloxacin 200 mg twice daily. Sensitivities can later guide therapy, which should last at least 28 days. Treat acute prostatitis energetically to avoid the development of chronic prostatitis. If acute urinary retention develops, drain by the suprapubic route. Adequate hydration is important (Walker and Wilson, 1999).

Chronic bacterial prostatitis

Antimicrobials that theoretically penetrate well into the prostate are lipid soluble, low protein binding with a high dissociation constant (pKa). These include azithromycin, doxycycline, erythromycin, minocycline, trimethoprim and the quinolones, among which ciprofloxacin has been the most studied. The organisms isolated in CBP are the same as in acute prostatitis.

The choice of antimicrobial should be guided by the above principles and by sensitivity test results. Recommended regimens include ciprofloxacin 500 mg twice daily, ofloxacin 200 mg twice daily or trimethoprim 200 mg twice daily (Walker and Wilson, 1999). Published trials usually describe treatment given for 4–6 weeks. In clinical practice better long-term results are obtained when treatment continues for at least 3 months.

Chronic non-bacterial prostatitis

There is no accepted evidence for the cause of CNBP so there is no firm basis for therapy. There is an argument that the inflammatory process itself may lead to obstruction of the ducts that drain foci of bacterial infection, thus preventing drainage by prostatic massage (Thin, 1997b). This is also supported by results of DNA amplification studies (Krieger et al, 1996b). On this basis many clinicians recommend the same antimicrobials as in CBP.

If there is a history of previous urethritis, then azithromycin, doxycycline, minocycline or erythromycin may be given. If there has been previous bacteruria, trimethoprim may be preferred. Again a 3-month course is advisable. A high fluid intake such as 3 litres per day and regular prostatic drainage by ejaculation also appear to help (Yamamoto et al, 1995). Constipation and diarrhoea should be avoided (Thin, 1997a).

Other suggestions include α-blockers, especially if there is a confirmed urodynamic abnormality. Pollen extract has been described as beneficial — it may be anti-inflammatory through prostaglandin synthesis inhibition and by antiadrenergic activity. Several reports have suggested benefit from transrectal or transurethral microwave hyperthermia. Non-steroidal anti-inflammatory agents may also help (Evans, 1994; Thin, 1997a).

Prostatodynia

Management of this condition can be challenging. Adequate hydration and prostatic drainage by ejaculation are advisable. Alpha blockers, non-steroidal anti-inflammatories and transurethral microwave hyperthermia have all been recommended (Evans, 1994; Neal and Moon, 1994; Thin, 1997a). Emotional and psychiatric conditions may need specialist management (Woodhouse and Rugg, 1984).

In all forms of chronic prostatitis minor exacerbations of symptoms may interrupt progress. Sometimes these may appear to follow periods of inadequate hydration, excess or infrequent ejaculation, or intercurrent illness, but frequently they appear for no obvious reason. It is important to support and reassure the patient that these exacerbations are transient. **HM**

Berguis JP, Heiman JR, Rothman I, Berger RE (1996) Psychological and physical factors involved in chronic idiopathic prostatitis. *J Psychosom Res* **41:** 313–25

Drach GW, Meares EM Jr, Fair WR, Stamey TA (1978) Classification of benign disease associated with prostatic pain: prostatitis or prostatodynia. *J Urol* **120:** 266

Evans DTP (1994) Treatment of chronic abacterial prostatitis: a review. *Int J STD & AIDS* **5:** 157–64

Eykyn S, Bultitude MI, Mayo ME, Lloyd Davies RW (1974) Prostatic calculi as a source of recurrent bacteriuria in the male. *Br J Urol* **46:** 527–32

Kirby RS, Lowe D, Bultitude M, Shuttleworth KED (1982) Intraprostatic urinary reflux; an aetiological factor in abacterial prostatitis. *Br J Urol* **54:** 729–31

Krieger JN, Egan KJ, Ross SO, Jacobs R, Berger RE (1996a) Chronic pelvic pains represent the most prominent urological symptom of 'chronic prostatitis'. *Urology* **48:** 715–22

Krieger JN, Riley DE, Roberts MC, Berger RE (1996b) Prokaryotic DNA sequences in patients with chronic idiopathic prostatitis. *J Clin Microbiol* **34:** 3120–8

Meares EM Jr (1987) Prostatitis. In: Chishom GD, Fair WR, eds. *Scientific Foundations of Urology.* 3rd edn. Heinemann, London: 373–8

Meares EM Jr, Stamey TA (1968) Bacterial localisation patterns in bacterial prostatitis and urethritis. *Invest Urol* **5:** 492–518

McNeal JE (1989) Anatomy and embryology. In: Fitzgerald JM, Krane RJ, eds. *The Prostate.* Churchill Livingstone, Edinburgh: 3–10

Neal DE, Moon TD (1994) Use of terazosin in prostatodynia and validation of a symptom score questionnaire. *Urology* **43:** 460–5

Nickel JC (1997) The pre and post massage test (PPMT); a simple screen for prostatitis. *Techniques Urol* **3:** 38–43

Noble J, Rickards D (1995) Developments in the radiological investigation of the lower urinary tract. *Int J STD & AIDS* **6:** 7–10

Thin RN (1997a) The chronic prostatitis syndromes. *J R Army Med Corps* **143:** 155–9

Thin RN (1997b) Diagnosis of chronic prostatitis: overview and update. *Int J STD & AIDS* **8:** 475–81

Walker P, Wilson J (1999) (UK National) Guidelines for the management of prostatitis. *Sex Trans Inf* **75**(Suppl): 546–50

Woodhouse CRJ, Rugg AJ (1984) Chronic perineal pain. *Br J Hosp Med* **32:** 302–4

Yamamoto M, Hibi H, Katsuno S, Miyake K (1995) Antibiotic and ejaculation treatments improve resolution rate of leukocytospermia in infertile men with prostatitis. *Nagoya J Med Sci* **58:** 41–5

KEY POINTS

- Acute prostatitis is diagnosed from symptoms, prostatic tenderness on rectal examination and urine culture. It responds well to antimicrobials.
- Chronic prostatitis has less clear clinical features.
- Diagnosis of chronic prostatitis depends on laboratory examination of expressed prostatic secretion and urine passed before and after prostatic massage.
- Chronic prostatitis can be differentiated into chronic bacterial prostatitis (CBP), chronic non-bacterial prostatitis (CNBP) and prostatodynia.
- CBP responds to appropriate antimicrobials.
- CNBP may respond to antimicrobials, anti-inflammatories and other measures.
- Prostatodynia — symptoms of prostatitis with no diagnostic findings — requires a variety of therapeutic measures including alpha blockers, regular ejaculation, high fluid intake and psychological support.
- Differential diagnosis of chronic prostatitis includes benign prostatic hypertrophy and carcinoma.