Chapter 8

URINARY TRACT INFECTIONS

These conditions have one common feature of significant bacteriuria.

CLASSIFICATION

A. Diseases with Bacteriuria:

1. Non obstructive.
2. Obstructive.
3. Neurogenic bladder.

B. Localization of Infection:

1. Upper UTI.
2. Lower UTI.
3. Superficial (cystitis).
4. Deep (pyelonephritis).

C. Duration of Infection:

1. Acute UTI.
2. Chronic UTI.

DEFINITIONS

1. Cystitis:

Infection limited to urinary bladder. Symptoms vary from severe pain on micturition, burning, frequency and dull pain over bladder area. Patients are usually afebrile.

Diagnosis of infection limited to bladder can not be accepted unless following minimal criteria are fulfilled:

1. Patient is afebrile.
2. Normal ESR.
3. Normal renal concentration capacity.
4. Antibodies against infecting organism.
5. Limitation of infection to bladder can be demonstrated by bladder wash and ureteral catheterization.

2. Acute Pyelonephritis:

Acute bacterial infection of renal parenchyma. Patient is febrile. Symptoms are toxic fever, chills, severe malaise, dysuria, urgency, frequency and loin pain.

Diagnosis is made from history and presence of bacteriuria and pyuria together with transitory lowering of renal concentration capacity, transitory increase of antibodies titre or demonstration of ureteral bacteriuria with bladder wash method.

3. Chronic Pyelonephritis:

Clinical condition characterized by continuous excretion of bacteriuria or frequent relapses of infection.

Radiologically there is characteristic progressive renal scarring.

Histologically there are characteristic lesions of renal parenchyma.

4. Cystourethral Syndrome:

Vague term used for patients with classical symptoms of cystitis but lacking demonstrable bacteriuria. Pyuria is often present. Some show inflammation on endoscopy. Condition is more common in small girls complaining of dysuria.

DIAGNOSTICS

Demonstration of significant bacteriuria is sole valid criterion for presence of UTI.

A. Demonstration of Bacteriuria:

Kass's suggestion for definition of significant bacteriuria:

1. Less than 10 raise to power 4 bacteria per ml of urine means probably contamination.
2. 10 raise to power 4 to 10 raise to power 5 bacteria per ml of urine suggests new culture.
3. More than 10 raise to power 5 bacteria per ml of urine indicates probably infection.
4. If urine is obtained by bladder puncture than 10 raise to power 3 bacteria per ml of urine is significant.

1. Collection of Urine:

1. Clean catch: Midstream urine should be collected. Preputial folds of small boys may contain large number of bacteria.
2. Bladder puncture: Mainly used in newborn or during first few days.

Indications:

i. Persistent bacteriuria of doubtful significance.
ii. Seriously ill patient in whom accurate diagnosis is essential.
iii. Obstruction of bladder outflow tract or urethra.

3. Catheterisation: This is used when bladder puncture is not convenient for example in children over 1 year. Risk of introducing infection for children with previous UTI is 50%.

2. Transportation of Urine:

Bacterial multiplication starts rapidly in vitro. At 0-4°C bacterial count will remain unchanged for 24-48 hours.

3. Influence of Antibiotics Present in Urine:

Therapy should be discontinued for sufficiently long time before culture to permit complete excretion of antimicrobials.

Lack of demonstration of significant bacteriuria in overt infection of urinary tract may be due to complete obstruction of unilaterally infected kidney or presence of antibiotics in urine.

B. Demonstration of Secondary Phenomenon of Inflammation:

1. WBC Count:

Appearance of increased number of white cells in urine is secondary to inflammation, bacterial or non bacterial. Pyuria thus never proves bacterial UTI nor does normal WBC count exclude UTI.

Pyuria is of diagnostic help in:

1. Making tentative diagnosis in acutely ill patients before results of culture are available.
2. Support of diagnosis of UTI in patients with asymptomatic bacteriuria.
3. Suggesting renal involvement by appearance of white cells casts.

It is more common to find normal WBC count in recurrent infection than first one. First specimen of urine in morning should be examined.

Quantitative evaluation of urinary white cells is made by counting cells of freshly voided uncentrifuged urine in counting chamber.

Voided specimen from boys should contain less than 10 WBC per cu mm. In girls 50-100 WBC per cu mm are normal.

Methylene blue 0.5% stain helps differentiate between WBC and epithelial cells.

Proteinuria is of little diagnostic help in UTI.

Haematuria is common especially in neonatal infection and in older boys.

2. Determination of Antibodies Titre:

Agglutinating and haemagglutinating antibodies to 'O' antigen of infecting E. Coli can be demonstrated in serum of patients with pyelonephritis but not from patients with superficial infection eg cystitis.

This characteristic is of help in knowing localization of infection which is of special interest in patients with asymptomatic bacteriuria or with symptoms suggesting cystitis where renal involvement is not infrequent although symptomalology is sparse. Antibodies are highly specific and thus can be used in diagnosis to verify that isolated bacteria are cause of infection. This may be clinically useful in patients with moderately high bacterial count (10 raise to power 4 to 10 raise to power 5 per ml of urine) and in all scientific work on UTI.

3. Renal Function Tests in UTI:

Renal concentration capacity: In acute infections of kidney there occurs transitory decrease of capacity of kidneys to concentrate urine. This may be used diagnostically to localize infection. In uncomplicated cases capacity is restored to normal in 6-8 weeks. If concentration capacity is not restored possibility of obstruction to urine flow, renal scarring or persistent infection should be considered.

Glomerular function: Increased blood urea is uncommon in uncomplicated acute UTI. If present it suggests either obstruction of urine flow with bilateral hydronephrosis or marked parenchymal reduction.

During newborn period blood urea increase may occur even in absence of obstruction. Lowering of renal blood flow during and after UTI may occur.

4. Radiology:

Aims of intravenous urogram and micturiting cystourethrogram are:

1. To detect factors predisposing to or encouraging infection consisting of congenital or acquired obstruction organic or functional of urinary flow, calculus and gross vesicoureteral reflux.
2. To detect and outline narrowing of renal tissue and calyceal dilatation which may be early sign of progressive renal scarring.
3. To check rate of growth of kidney which may be valuable aid in assessing effect of treatment.

Apparent First Infection:

Immediate and full radiologic investigation is mandatory in following situations:

1. When mass is seen or palpated after micturition in area over symphysis suggesting obstructed bladder emptying.
2. When mass is palpated in upper abdomen suggesting hydronephrosis.
3. When increased blood urea or serum creatinine has been found.
4. When increased blood pressure is recorded.
5. When infection does not clear inspite of adequate antibiotics.
6. When there is persistently low concentration capacity or persistently high antibodies titre.

7. All boys with UTI.
8. All girls below 3-4 years of age.

Recurrent Infection:

Patients of all age and gender should have intravenous urogram and micturiting cystourethrogram. They can be repeated in order to monitor renal growth and calyceal appearance at intervals of six months during first year of life, at intervals of 12 months during second year of life and later on at intervals of 2-3 years.

5. Other Diagnostic Studies:

1. Cystoscopy.
2. Haemodynamic studies of act of micturition.
3. Isotope renography.
4. Ultrasonography.

ETIOLOGY

Enteric bacteria cause majority of UTI in patients who have no complicating disorder of urinary tract (calculus, obstruction and neurogenic bladder).

E. Coli group 'O' (1, 2, 4, 6, 7, 18, 75) which dominate faecal flora are also subgroup which invade urinary tract.

First few months after sulphonamide course further UTI is often sulphonamide resistant. This is due to antibiotic induced change in intestinal flora. This then determines bacteriology of reinfection.

In patients with complications such as calculus, obstruction or neurogenic bladder, E. Coli infection is common but other gram negative bacteria such as proteus mirabilis, pseudomonas aeruginosa, alkaligenus faecalis, klebsiella aerogenes, staphyllococcus albus, staphyllococcus aureus and enterococci are found. These bacteria have complicated resistance pattern. These bacteria dominate urethral flora.

PATHOGENESIS

There are two routes for entry of bacteria in urinary tract. Ascending and haematogenous. Most infections are ascending but those in newborns are blood born.

1. Haematogenous Route:

Bacterimia in newborns may be caused by different manipulations eg pharyngeal suction, tracheal tubes, umbilical catheterization etc. or may have started prenatally.

2. Ascending Infection:

Close proximity of urinary tract to anal area with its heavy colonization by gram negative organisms presupposes highly efficient defense mechanism to prevent ascending infection.

Clearing of bacteria entering urinary tract are related to two factors. Ability to complete emptying of urinary system and bactericidal element present in bladder.

In patient with posterior urethral valve, ureterocele, bladder diverticulum, neurogenic bladder or calculus, emptying mechanism is at fault.

Young girls with UTI without malformations have more or less continuous bacteriuria. Recurrent infection in them is new infection (reinfection), not recrudescence of old one (relapse). Bacterial colonization of periurethral area and vagina precedes bladder infection. It is also seen that urogenital cells from UTI prone females bind E. Coli better than cells from controls. This suggests defective host resistance.

Vesicoureteric reflux has been especially incriminated as factor facilitating infection in these patients. There are two phases in initiation of ascending infection. Invasion of bladder and spread of bacteria from bladder to renal tissue.

Factors influencing acquisition of infection:

1. Gender: There is male preponderance during first weeks of life which later converts to female one.
2. Age: Onset of UTI has peak incidence during first year of life.
3. Cooling may provoke urgency.
4. Acute respiratory infection precedes UTI in 10-15% cases.
5. Dark complexion girls are more prone for UTI than white ones.

Pathogenesis of Symptoms:

There is tendency for symptoms to become less and less dramatic with increasing number of attacks.

Several symptoms of UTI (high fever, chills, malaise, leucocytosis) are caused by lipopolysaccharides (endotoxin) liberated from bacteria. Repeated exposures to endotoxin seems to induce relative tolerance and fever and leucocytosis are not elicited with same ease. This asymptomatic UTI may be expression of such tolerance phenomenon. This tolerance is only relative since with high dose of endotoxin tolerance may be overcome and generalized symptoms develop.

CLINICAL FEATURES

In Neonate

Asymptomatic bacteriuria is found in 1-3% of newborns, mainly in males. In some it persists if untreated and eventually cause overt findings and symptoms after 1-2 months or more.

Classical symptoms of neonatal UTI are sluggishness, feeding difficulty, irritability, tenderness upon touching, poor weight gain with or without fever.

In 75% of neonates falling ill during first 10 days of life there is early drop in weight exceeding 10% of birth weight (primary weight loss) or fall in

weight of 50 grams or more occuring at days 5-10 usually after preceding weight gain (secondary weight loss). Abnormally slow weight gain may be noted after successful treatment.

Overt neurological symptoms such as generalized convulsions, marked hypotonicity, irritability, respiratory inadequacy, absent or hardly elicitable primitive reflexes are seen in 25% of patients.

Pleocytosis of CSF without meningitis is found in several patients with and without cerebral symptoms.

Laboratory investigations reveal bacterimia in 50% cases. Blood urea increased in 20% cases. Some have marked oliguria and transient increase in renal size.

In Infants and Toddler

Acute infections especially first ones present with high remitting fever. Meningismus, irritability, abnormal sensitivity to touching skin are often seen. Abdominal pain, vomiting and pallor or grey skin color is common. Symptoms of UTI are lacking but typically smelly odors of napkin may attract mother's attention. Few patients may have microscopic haematuria. Inability to thrive, anorexia, vomiting, poor weight gain, sluggishness, diffuse abdominal discomfort are seen in long standing infections.

Lack of more dramatic symptoms may be due to tolerance to endotoxin.

In Adolescent Girls

Symptoms become more moderate with increasing age. High fever may appear with rigors. Urinary symptoms may become more frequent from age 6-7 years but may be completely lacking upto puberty. Abdominal discomfort is common. Localization of pain to loin is phenomenon appearing late. Tenderness over loin is noted. Moderate character of symptoms may be due to fact that infections in this age group are recurrences to large extent with possible endotoxin tolerance.

In Adolescent Boys

There are few general symptoms. Fever is seen in only 50% cases. It is moderate. Haematuria may be present with dysuria and urgency. Proteus and atypical bacteria are frequent causative organisms. Renal concentration capacity is lowered.

Infections Complicated by Obstruction

When occurring with bilateral hydronephrosis, infections usually start during first few months of life.

With other obstructions onset of infections may be at any age.

On examination enlarged bladder or mass in loin may be found. Hypertension, dehydration, electrolyte disturbances including acidosis are seen.

Straining at micturition, poor urinary stream or dribbling after micturition may characterize urethral obstruction.

SUMMARY OF CLINICAL FEATURES

1. Febrile urinary tract infection is always pyelonephritis but patients of pyelonephritis may be afebrile and asymptomatic.
2. More infections patients have had previously or closer recurrence follows earlier infection less severe are general symptoms. This may be because of acquired relative tolerance to effect of endotoxin.
3. Diagnosis of cystitis can not be made only on basis of symptomatology.
4. Such bacteria as enterococci, proteus, pseudomonas and staphyllococci often cause less symptoms than infections caused by E. Coli.
5. Increased blood urea and blood pressure in patients above age of one month means existence of bilateral hydronephrosis or advanced renal parenchymal reduction.
6. In children with symptoms of urgency, burning, dysuria or diurnal enuresis of secondary onset urine may often be sterile inspite of pyuria. This suggests inflammation of urinary or genital tract or urogenital tuberculosis.

ASYMPTOMATIC BACTERIURIA

In healthy girls aged 4-16 years prevalence of bacteriuria is 0.7-2.5%. There is no definitive increase with age. In males prevalence is very low beyond neonatal period.

Clinical Features:

One third of patients have past history with symptoms referrable to urinary tract. Pyuria is absent. Reflux is seen in 25-30%. Focal renal scar occurs in 10-25%.

Bacteriology:

E. Coli isolates from patients with symptomatic pyelonephritis are different than those from asymptomatic bacteriuria. Some of differences may be due to selection of polysaccharide deficient mutant as adaptation of infection to local immune response of host. After elimination of these mutants by therapy urinary tract may be invaded by intact bacteria from faecal reservoir which may explain why therapy in asymptomatic bacteriuria sometimes is followed by symptomatic recurrences.

Diagnosis:

C reactive protein may be more reliable than wash out tests, elevation of ESR, reduction in concentration capacity and antibodies titre determination.

Therapy:

7-10 day course of antibiotic temporarily eliminates infection in 90% cases but only 20-25% remain uninfected one two two years later.

Spontaneous cases persisting for one year appear in 10% cases.

It seems reasonable to treat and follow patients with symptoms, with foul smelling urine, with scars and with gross reflux.

Course:

Asymptomatic bacteriuria is consequence of earlier symptomatic infections. It is better to screen infants and small children with fever for urinary tract infections.

MANAGEMENT

Febrile UTI in child is inflammatory, probably abscess forming process in renal parenchyma. Consequently every infection must be regarded as potential threat to future health of child.

Aim of therapy is to prevent progressive renal disease. This implies responsibility for several years for each patient with definite infection.

Predisposing factor such as congenital or acquired obstruction or stone should be searched for. Inspect organs, abdomen and bladder area and palpate thoroughly. Raised bladder, mass in loin, hypertension, high blood urea, electrolyte disturbances including acidosis should evoke suspicion of complication. Response to therapy should be judged. If fever does not settle or sediments do not clear in 4-5 days after institution of therapy it is likely that either bacteria are resistant to antibiotic or that there is complication. Same is true if concentration capacity does not return to normal after 6 weeks. Such patients should have intravenous urogram or voiding cysto urethro gram as soon as possible.

If urethral obstruction is suspected on initial examination, patient should have drainage by urethral catheter until thorough evaluation can be performed.

If radiological examination shows marked dilatation of upper urinary tract, catheter should be left in place until free urinary flow is established surgically. Direct drainage of unilateral obstructed pelvis may be necessary.

ANTIBIOTIC THERAPY

Current approach is to seek eradication of infection by course of antibiotic for 10-14 days and follow this by prophylactic antibiotic therapy in smaller dose given over longer interval.

Chronic parenchymal infections require bactericidal antibiotic in high doses over long time by intravenous route.

Urinary concentration of antibiotic is more important than blood concentration.

Nitrofurantoin when given in doses less than 3 mg per kg per day is well tolerated. Pulmonary fibrosis is rare. When GFR falls below 50% of normal nitrofurantoin becomes ineffective.

Cotrimoxazole dose 5-7 mg trimethoprim and 25-35 mg sulphamethoxazole per kg twice daily for 12 days.

When patient is vomiting or seriously ill cephalosporin third generation (ceftriaxone or cefotaxim) 50-75 mg per kg per day intravenous is given.

Urine culture should be sent after 3 days to check for possible return of bacteriuria. Urine culture should be repeated after 3 weeks.

Sulphonamides reach high concentration in gut which exerts selective effect on fecal flora favoring colonization by sulphonamide resistant strains. Since gut flora in most instances determines bacteriology of urinary tract infections, these can be anticipated as likely to be resistant. New bacteria may be resistant to not only sulphonamides but also other antibiotics. Bacteria transfer resistance to new bacteria. This is known as transmissible resistance and is accomplished by plasmids, extra chromosomal DNA, carrying genetic code for different properties including drug resistance (R factor). Bacteria carrying resistance of transmissible type are more viable than those carrying resistance of traditional mutation. They also carry virulence factor.

Problem of resistant urinary tract infections should be seen in light of influence of therapy on intestinal flora. Use of more and more potent antibiotic may induce more profound changes in intestinal flora and so more and more complicated resistance patterns of multiple resistance types of bacteria causing recurrent infections. Best protection against urinary re infection would be offered by preparation combining good antibacterial effect on urinary tract with no propensity for selecting resistant intestinal strains. Cotrimoxazole seems to fullfill these requirements.

VESICOURETERIC REFLUX

VUR is pathological phenomenon except during first few weeks of life. It may be congenital or acquired and in some instances possibly genetically determined. There are grades depending upon whether reflux takes place during rest or only on voiding.

VUR has two effects: It may facilitate recurrent infection by preventing complete emptying of bladder and predispose to renal scarring by effectively transporting bacteria from bladder upto kidney tissue.

When gross VUR is associated with intra renal reflux and infection it is predictive of future renal damage in area with IRR.

Anatomical Basis for IRR:

Collecting ducts open with slit like orifices on cone shaped single papillae but with circular ones in fused papillae. With increasing pressure in renal pelvis slit like orifices tend to be occluded while gaping orifices of fused papillae remain open and urine is forced into renal parenchyma. Since fused papillae with gaping orifices are not always present gross VUR is not invariably associated with renal damage.

Since distribution of fused papillae is most common in upper pole followed by lower and least common in mid zone of kidney, scarring is also seen in these areas only.

Renal scarring has multifactorial background. IRR being one important factor. Age of onset of infection, delay of therapy and quality of follow up are other factors.

Some E. Coli strains regularly cause ureteritis leading to dysfunction with increased intra ureteral pressure and massive pyelorenal backflow with renal infection. This functional obstruction is as effective as gross VUR with IRR in causing renal damage. E. Coli which cause ureteral dysfunction belong to group with binding to P blood group associated antigen.

There is tendency for reflux to disappear spontaneously. Hence 2-3 years prophylactic antibiotic therapy (nitrofurantoin 1-2 mg per kg per day) is given before considering surgery.

PROGNOSIS

Infections complicated by obstruction: Nature of obstruction, success of surgical intervention and time lapse between onset of infection and establishment of adequate drainage determine degree of permanent damage to kidney.

Girls without obstruction falling ill after newborn period: They are liable to get recurrences, usually reinfections. Tendency for repeated infections may persist for years. Long term follow up is required since recurrences are asymptomatic.

Clinically severe complications: Most severe manifestations of UTI are uraemia, papillary necrosis, calculus, anaemia, hypertension. They are due to renal scarring.

Neonatal infection without obstruction: These tend to part of generalized bacterimia. Early recurrences during month following initial infection appear in 25% cases. Recurrence after 1 year is rare. Frequency of renal scarring after neonatal UTI is 5%.

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