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TITLE: **ACUTE AND CHRONIC PYELONEPHRITIS**

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ACUTE AND CHRONIC PYELONEPHRITIS

Definitions

Acute pyelonephritis (APN) is an acute, nonspecific, infectious (most often bacterial) unilateral or bilateral tubulointerstitial disease, which clinical syndrome includes flank pain, renal tenderness, fever and chills, accompanied by bacteriuria.

Chronic pyelonephritis (CPN) is a disease of renal cavity sys-tem (pelvis and calyces), underlying parenchyma (tubulointerstitial system) caused of bacterial infection with longtime course, inclu-ding periods of exacerbations and remissions, progressing in some cases to CRF.

Etiology

Bacteria are the leading cause for UTI. *Escherichia coli* is res-ponsible for 75% of community-acquired UTI. Several organism characteristics have been associated with renal invasion including belonging to a restricted number of O:K:H serotypes, production of hemolysin, resistance to the bacterial activity of normal human se-rum and the presence of adhesion proteins that bind to receptors of epithelial cells

Other gram-negative rods, including *Klebsiella* species, *Proteus* species, *Pseudomonas aeruginosa* and *Enterobacter* species are isolated from 10-15% of patients with UTI. *Proteus mirabilis* very rapidly invades the upper urinary tract and predisposes struvite calculi formation. *Coagulase-negative staphylococci* and *Enterobacter* cause 2-4% of UTI. Rare causes for UTI are *Staphylococcus saprophyticus, Streptococci group A, Neisseria* and *Haemophilus influenzae*. *Staphylococcus aureus* infection commonly occurs in patients with bacteremic staphylococcus infection.

Pathogenesis

Three primary routes postulated for the migration of bacteria to the kidneys are bloodstream, lymphatics and ascendancy through the urinary tract. The ascending route via urethra, bladder and ureter to the pelvis and parenchyma appears to be the principal pathway.

Bacteria and most common pathogen fecal / *E. coli* migrate from the perianal skin to colonize the vaginal introitus and urethra. The microorganisms then ascend hrough the urethra into the bladder and in cases of APN from the bladder to the kidney via ureters.

Both bacterial and host factors are important in predisposing to acute UTI. Behavioral factors such as not voiding after intercourse, or postponing voiding also appear to increase the risk of infection. Uropathogenic *E. coli* appears to posses specific virulence determinants such as fimbriae or production of *hemolysin* or *aerobactin* that enable them to colonize and infect UT more efficiently than strains lacking these virulence factors.

Rarely the kidneys are infected secondary to bacteremia.

Predisposing factors: The obstruction of urine flow or other functional abnormalities of UT impair the normally efficient ability of the bladder to eliminate bacteria. Instrumentation of UT, particular-ly catheterization provide a portal of entry for bacteria and also ma-kes it more difficult to eradicate bacteria with drugs. Vesicoureteral reflux may facilitate the ease /i:z/, with which bladder bacteria can ascend to the kidney. Interestingly the most bacteria, causing complicated urinary infection lack the specific urovirulence determinant characteristic of strains causing uncomplicated UTI, suggesting, that their pathogenicity relates mainly to host impairment.

Predisposing and defence factors

Local host defence

Length of male urethra

Prostatic antibacterial factor

Normal vaginal flora

Cervicovaginal antibody production

Voiding mechanism

Bladder surface glycosaminoglycan

Competent vesicoureteral valves

Renal capacity for urinary acidification, concentration and ammoniagenesis

Tamm-Horsfall mucoprotein

Urinary opsonic activity

ABO blood group secretion

Local predisposing factors

Prostatic adenoma or carcinoma

Renal or bladder calculi

Pregnancy

Strictures of ureters juri:tъ:s/

Primary or metastatic malignancy

Retroperitoneal fibrosis

Cysts

Nephrocalcinosis

Uric acid nephropathy

Renal parenchymal scarring

Microorganism virulence /virulъns/ factors

Pili (fimbriae) attachment mechanisms

K-mechanism

Urease production

Hemolysin production

Aerobactin production

Motility

Capacity to form protoplasts

Pathology

The hallmark of APN includes abscess formation and edema of the renal parenchyma and accumulation of polymorphonuclear leu-cocytes around tubules. In general glomeruli are spared, though small abscesses may surround them. Areas of infection are cha-racterristically wedge-shaped, with the apex in the medulla resembling an infarct. Tissue destruction is greater in cortex than in medulla.

Histologic features can overlap between APN and CPN. The relative degree of edema and fibrosis rather than the interstitial cellular response is the most useful criteria/ to delineate these entities.

In CPN fibrosis with atrophy of overlying renal tissue leads to surface depression or scars. A sharply defined border between normal and diseased tissue is characteristic. The two kidneys are markedly asymmetrically involved. The capsule is adherent /adhiъrant/ and the cortical surface irregular. Calyceal clubbing results from papillary retraction into the scar. Dilatation, muscular hypertrophy, fibrosis inflammatory thickening of the calyceal system occur in a variable extent.

Clinical manifestations

APN characteristically presents with localized flank, low-back or abdominal pain accompanied by generalized constitutional symp-toms as fever, chills, sweats, headache, myalgia, nausea, vomi-ting, and malaise. Symptoms of lower UTI may or may not be pre-sent. The illness may progress very rapidly and many patients seek care within 1 to 3 hours of onset of symptoms. The renal pain may radiate to the epigastrium or the lower abdominal quadrants. Severe flank pain with radiation to the groin is unusual and suggests ureteral obstruction. Gastrointestinal symptoms predominate in about 10% of patients. Meningismus may be a primarily presenting feature. Some patients may be severely ill, while other may have only low-grade fever and mild flank discomfort. The severity of illness associated with APN ranges from very mild to quite severe, including Gram-negative septicemia, and necrotizing papilitis or perinephric abscesses.

Diagnosis

The suspected diagnosis of acute lower UTI can be readily confirmed by microscopic examination of the urine and urine culture. Culture of midstream urine will generally demonstrate the

etiologic bacterial agent in concentrations more than 10^5 cfu/ml. However in one-third of cases colony counts will range from 10^2 to 10^4 colony-forming units per milliliter.

The clinical diagnosis of renal infection requires traditionally the presence of flank pain, renal-angle tenderness, fever over 38°C, a positive urine examination for pyuria and bacteriuria, and leukocy-tosis. The presence of leukocyte casts in a fresh voided specimen of urine strongly supports the diagnosis, but casts are demonstrable in only 20 to 40% of cases.

The evidence of some anatomical UT abnormality is a key to distinct complicated UTI. Evaluation for reflux or other defects should be strongly considered in children with recurrent UTI infections. Men in age over 50 are suspected to have a bladder outlet obstruction, particularly prostatic adenoma.

Intravenous pyelography and US are usually normal in APN. It could be present renal enlargement, delayed excretion of contrast material, narrowing and elongation of collecting system. In *chronic pyelonephritis* there may be an irregular cortical scar, club-bed calyx, impaired visualization of the kidneys. Renal contraction also is usually seen and is characteristically asymmetrical. Sono-graphy can demonstrate decreased renal size, cortical irregularity and increased echogenicity.

Treatment

Patients with significant symptoms should be hospitalized for initial investigation and parenteral antibacterial treatment. Intrave-nous fluids, analgesics, and bed rest are usually prescribed during the initial 48-72 hours. In 80% of patients improvement occurs within 72 hours. Oral therapy should be used after the first 7 days of treatment.

Selection of antimicrobials for treatment of *complicated UTI* should take into account the relatively broad array of bacterial species, that cause such infections and the degree of illness.

1. Antibiotic – 10 days, in all cases with microbiologic urine examination; After finishing the course – in three consecutive days – urine cultures; If they are sterile: 2. Sulphonamide – 10 days; in 3 consecutive day – urine cultures. 3. Quinolones – 7-10 days. In cases when the antibiotical therapy is not effective and in the urine grow bacteria in an account more than 10^5 mfu/ml, should be started a new course with a different antibiotic for 7-10 days.

The agents of choice in treatment of UTI are gentamicin – 2 mg/kg, chloramphenicol – 2 g/d, ampicillin (without or with sulbac-tam) – 3-6 g, amoxicillin with or without clavulanic acid) – 2-4 g/d, cefalosporins – cephazolin – 3-6 g/d, ceftriaxon – 2-6 g/d, cefu-roxime – 1,5-3,0 g/d. In cases of complicated UTI may be taken in account imipenem-cilastatin, meropenem, maxipim. In case of so called methicillin-resistant staphylococcal infection – vankomycin and teicoplanin.

In the group of sulphonamides the choice is not vast – trimethoprim-sulfamethoxazole 1920 mg/d. The group of quinolones includes pefloxacin, ciprofloxacin, norfloxacin, ofloxacin, enoxacin, lomefloxacin in a daily dose 400-500-800 mg.

The total required duration of therapy to achieve optimal cure rates in patients with APN is uncertain. The duration of therapy ranges between 21 and 35 days. The minimum two weeks is re-commended. Prolonged therapy may be needed for patients with urinary calculi, urinary flow obstruction or unremoved other predis-posing factor. Infection usually cannot be eradicated without removal the calculi (chirurgical, spontaneous or by lithotripsy).

Prevention

Urinary catheter should not be used without medical indications. Sterile insertion and maintenance of a closed catheter system can reduce the incidence of related infections.

Antibiotic prophylaxis has no value on chronically catheterized patients. It should be provided to patients undergoing prostatic or other urologic surgery. All pregnant women should be screened for bacteria in the first trimester and treated if positive.

The prophylaxis of lower and as well upper UTI with trimethoprim-sulfamethoxazole in women, in transplanted patients, and children with vesicoureteral reflux reduces the incidence of recur-rent infection.

Immunization has been suggested as an alternative of chemo-prophylaxis. Both capsular antigen and pili have been used to pre-vent ascending infection in animal models.