Kidney diseases

Lecture 7

Diseases of Glomerulus

DEFINITION AND CLASSIFICATION

Glomerular diseases encompass a large and clinically significant group of renal diseases. Glomerulonephritis (GN) or Bright's disease is the term used for diseases that primarily involve the renal glomeruli. It is convenient to classify glomerular diseases into 2 broad groups:

I. PRIMARY GLOMERULONEPHRITIS

1. Acute GN i) Post-streptococcal ii) Non-streptococcal
2. Rapidly progressive GN
3. Membranous GN
4. Focal and diffuse proliferative GN
5. Chronic glomerulonephritis

II. SECONDARY SYSTEMIC GLOMERULAR DISEASES

1. Lupus nephritis (SLE) 2. Diabetic nephropathy 3. Amyloidosis 4. Systemic infectious diseases (bacterial e.g. bacterial endocarditis, syphilis ; viral e.g. HBV, HCV, HIV ; parasitic e.g. falciparum malaria)

CLINICAL MANIFESTATIONS The clinical presentation of glomerular disease is quite variable but in general four features—proteinuria, haematuria, hypertension and disturbed excretory function, are present in varying combinations depending upon the underlying condition. A firm diagnosis, however, can be established by examination of renal biopsy under light, electron and immunofluorescence microscopy. Following six major glomerular syndromes are commonly found in different glomerular diseases:

I. ACUTE NEPHRITIC SYNDROME This is the acute onset of microscopic haematuria, mild proteinuria, hypertension, oedema and oliguria following an infective illness about 10 to 20 days earlier. The underlying causes of acute nephritic syndrome may be primary glomerulonephritic diseases or certain systemic diseases.

II. NEPHROTIC SYNDROME In children, primary glomerulonephritis is the cause in majority of cases of the nephrotic syndrome; most frequent being lipoid nephrosis (65%).

In adults, on the other hand, systemic diseases (diabetes,amyloidosis and SLE) are more frequent causes of nephrotic syndrome. The most common primary glomerular disease in adults is membranous glomerulonephritis (40%).

III. ACUTE RENAL FAILURE Acute renal failure (ARF) is characterized by rapid decline in renal function. ARF has many causes including glomerular disease, principally rapidly progressive GN and acute diffuse proliferative GN.

IV. CHRONIC RENAL FAILURE These cases have advanced renal impairment progressing over years and is detected by significant proteinuria, haematuria, hypertension and azotaemia. Such patients generally have small contracted kidneys due to chronic glomerulonephritis.

V. ASYMPTOMATIC PROTEINURIA Presence of proteinuria Unexpectedly in a patient may be unrelated to renal disease (e.g. exercise-induced), or may indicate an underlying mild glomerulonephritis.

VI. ASYMPTOMATIC HAEMATURIA Asymptomatic Microscopic haematuria is common in children and young adolescents and has many diverse causes such as diseases of the glomerulus, renal interstitium, calyceal system, ureter, bladder, prostate, urethra, and underlying bleeding disorder, congenital abnormalities of the kidneys or neoplasia.

Diseases of Tubules

TUBULAR AND TUBULOINTERSTITIAL DISEASES

This group parenchymal of diseases is discussed under 2 headings:

I. Primary tubular diseases that include tubular injury by ischaemic or toxic agents i.e. acute tubular necrosis.

II. Tubulointerstitial diseases that include inflammatory involvement of the tubules and the interstitium i.e. pyelonephritis (acute and chronic).

ACUTE TUBULAR NECROSIS

Acute tubular necrosis (ATN) is the term used for acute renal failure (ARF) resulting from destruction of tubular epithelial cells. ATN is the most common and most important cause of ARF characterised by sudden cessation of renal function. Based on etiology and morphology, two forms of ATN are distinguished—ischaemic and toxic; however both forms have a somewhat common pathogenesis.

TUBULOINTERSTITIAL DISEASES The term tubulointerstitial nephritis is used for inflammatory process that predominantly involves the renal interstitial tissue and is usually accompanied by some degree of tubular damage

ACUTE PYELONEPHRITIS

Acute pyelonephritis is an acute suppurative inflammation of the kidney caused by pyogenic bacteria.

ETIOPATHOGENESIS Most cases of acute pyelonephritis follow infection of the lower urinary tract. The most common pathogenic organism in urinary tract Infection (UTI) is Escherichia coli (in 90% of cases) . The bacteria gain entry into the urinary tract, and then into the kidney by one of the two routes:

1. Ascending infection This is the most common route of infection. The common pathogenic organisms are inhabitants of the colon and may cause faecal contamination of the urethral orifice, especially in females in reproductive age group

2. Haematogenous infection Less often, acute pyelonephritis May result from blood-borne spread of infection. This occurs more often in patients with obstructive lesions in the urinary tract, and in debilitated or immunosuppressed patients

CHRONIC PYELONEPHRITIS

Chronic pyelonephritis is a chronic tubulointerstitial disease resulting from repeated attacks of inflammation and scarring.

ETIOPATHOGENESIS Depending upon the etiology and pathogenesis, two types of chronic pyelonephritis are described.

1. Reflux nephropathy Reflux of urine from the bladder into one or both the ureters during micturition is the major cause of chronic pyelonephritis. Vesicoureteric reflux is particularly common in children, especially in girls.

2. Obstructive pyelonephritis Obstruction to the outflow of urine at different levels predisposes the kidney to infection. Recurrent episodes of such obstruction and infection result in renal damage and scarring.

OBSTRUCTIVE UROPATHY

Obstruction in the urinary tract is common and important because it increases the susceptibility to infection and stone formation. Obstruction can occur at any age and in either sex. The cause of obstruction may lie at any level of the urinary tract—renal pelvis, ureters, urinary bladder and urethra. The obstruction at any of these anatomic locations may be intraluminal, intramural or extramural as under: A. INTRALUMINAL : 1. Calculi 2. Tumours (e.g. cancer of kidney and bladder) 3. Sloughed renal papilla 4. Blood clots 5. Foreign body

B. INTRAMURAL : 1. Pelvi-ureteric junction (PUJ) obstruction 2. Vesicoureteric obstruction 3. Urethral stricture 4. Urethral valves 5. Inflammation 6. Neuromuscular dysfunction

C.EXTRAMURAL 1.Pregnant uterus 2.Retroperitoneal fibrosis 3.Tumours (e.g. carcinoma of cervix, rectum, colon, caecum etc) 4. Prostatic enlargement, prostatic carcinoma and prostatitis 5. Trauma

The obstruction may be unilateral or bilateral, partial or complete, sudden or insidious. There are three important anatomic sequelae of obstruction, namely: hydronephrosis, hydroureter and hypertrophy of the bladder

NEPHROLITHIASIS

Nephrolithiasis or urolithiasis is formation of urinary calculi at any level of the urinary tract. Renal calculi are characterized clinically by colicky pain (renal colic) as they pass down along the ureter and manifest by haematuria.

TYPES OF URINARY CALCULI

There are 4 main types of urinary calculi:

1. CALCIUM STONES Calcium stones are the most common comprising about 75% of all urinary calculi. They may be pure stones of calcium oxalate (50%) or calcium phosphate (5%), or mixture of calcium oxalate and calcium phosphate (45%). Etiology It is variable. Morphology Calcium stones are usually small (less than a centimeter), ovoid, hard, with granular rough surface.

2. MIXED (STRUVITE) STONES About 15% of urinary calculi are made of magnesium-ammonium-calcium phosphate, often called struvite; hence mixed stones are also called as ‘struvite stones’ or ‘triple phosphate stones’. Etiology Struvite stones are formed as a result of infection of the urinary tract with urea-splitting organisms that produce urease such as by species of Proteus, and occasionally Klebsiella, Pseudomonas and Enterobacter. These are, therefore, also known as infection-induced stones. However, E. coli does not form urease.

Morphology Struvite stones are yellow-white or grey. They tend to be soft and friable and irregular in shape. ‘Staghorn stone’ which is a large, solitary stone that takes the shape of the renal pelvis where it is often formed is an example of struvite stone.

3. URIC ACID STONES Approximately 6% of urinary calculi are made of uric acid. Uric acid calculi are radiolucent unlike radio-opaque calcium stones

4. CYSTINE STONES Cystine stones comprise less than 2% of urinary calculi. Morphology Cystine stones are small, rounded, smooth and often multiple

HYDRONEPHROSIS Hydronephrosis is the term used for dilatation of renal pelvis and calyces due to partial or intermittent obstruction to the outflow of urine. Hydronephrosis develops if one or both the pelviureteric sphincters are incompetent, as otherwise there will be dilatation and hypertrophy of the urinary bladder but nohydronephrosis. Hydroureter nearly always accompanies hydronephrosis. Hydronephrosis may be unilateral or bilateral.

UNILATERAL HYDRONEPHROSIS This occurs due to some form of ureteral obstruction at the level of pelviureteric junction (PUJ). The causes are:

1. Intraluminal e.g. a calculus in the ureter or renal pelvis.
2. Intramural e.g. congenital PUJ obstruction, atresia of ureter, inflammatory stricture, trauma, neoplasm of ureter or bladder.
3. Extramural e.g. obstruction of upper part of the ureter by inferior renal artery or vein, pressure on ureter from outside such as carcinoma cervix, prostate, rectum, colon or caecum and retroperitoneal fibrosis.

BILATERAL HYDRONEPHROSIS This is generally the result of some form of urethral obstruction but can occur from the various causes listed above if the lesions involve both sides. Based on this, hydronephrosis may be of following types:

1. Congenital e.g. atresia of the urethral meatus, congenital posterior urethral valve.
2. Acquired e.g. bladder tumour involving both ureteric orifices, prostatic enlargement, prostatic carcinoma and prostatitis, bladder neck stenosis, inflammatory or traumatic urethral stricture .

RENAL VASCULAR DISEASES

HYPERTENSIVE VASCULAR DISEASE

A persistent and sustained high blood pressure has damaging effects on the heart (e.g. hypertensive heart disease),
brain (e.g. cerebrovascular accident or stroke) and kidneys (benign and malignant nephrosclerosis).

DEFINITION AND CLASSIFICATION

Criteria for normal blood pressure, prehypertension And hypertension (stage 1 and stage 2) have been laid by the National Institutes of Health (NIH), US as below:

CATEGORY	SYSTOLIC (mmHg)	DIASTOLIC (mmHg)
Normal	< 120	and < 80
Prehypertension	120-139	or 80-89
Hypertension		
Stage 1	140-159	or 90-99
Stage 2	>160	or >100
Isolated systolic hypertension	≥140	and < 90
Malignant hypertension	> 200 (sudden onset)	≥ 140 (sudden onset)

Hypertension is generally classified into :

1. Primary or essential hypertension in which the cause of increase in blood pressure is unknown. Essential hypertension constitutes about 80- 95% patients of hypertension.
2. Secondary hypertension in which the increase in blood pressure is caused by diseases of the kidneys, endocrines or some other organs. Secondary hypertension comprises remaining 5-20% cases of hypertension. According to the clinical course, both essential and secondary hypertension may be benign or malignant.

Benign hypertension is moderate elevation of blood pressure and the rise is slow over the years. About 90-95% patients of hypertension have benign hypertension.

Malignant hypertension is marked and sudden increase of blood pressure to 200/140 mmHg or more in a known case of hypertension or in a previously normotensive individual; the patients develop papilloedema, retinal hemorrhages and hypertensive encephalopathy.

ETIOLOGY AND PATHOGENESIS

In general, normal blood pressure is regulated by 2 haemodynamic forces—cardiac output and total peripheral vascular resistance.

ESSENTIAL (PRIMARY) HYPERTENSION A number of factors are related to its development.

1. Genetic factors.
2. Racial and environmental factors.
3. Risk factors modifying the course of essential hypertension i) Age, Younger the age at which hypertension is first noted but left untreated, lower the life expectancy. ii) Sex , Females with hypertension appear to do better than males. iii) Atherosclerosis . iv) Other risk factors e.g. smoking, excess of alcohol intake, diabetes mellitus.

SECONDARY HYPERTENSION The mechanisms of this less common type are better known.

1. Renal hypertension : Hypertension produced by renal diseases is called renal hypertension. Renal hypertension is subdivided into 2 groups:

i) Renal vascular hypertension . ii) Renal parenchymal hypertension.

In either case, renal hypertension can be produced by one of the following three inter-related pathogenetic mechanisms:

a) Activation of renin-angiotensin system

c) Release of vasodepressor material

b) Sodium and water retention

2. Endocrine hypertension A number of hormonal secretions may produce secondary hypertension as follows:

i) Adrenal gland—e.g. Cushing's syndrome, and pheochromocytoma.

ii) Parathyroid gland—e.g. hypercalcaemia in hyperparathyroidism.

iii) Oral contraceptives.

3. Coarctation of aorta.
4. Neurogenic Psychogenic .

EFFECTS OF HYPERTENSION Systemic hypertension causes major effects in three main organs—heart and its blood vessels, nervous system, and kidneys. An important and early clinical marker for renal injury from hypertension and risk factor for cardiovascular disease is macroalbuminuria (i.e. albuminuria > 150 mg/ day or random urine albumin/creatinine ratio of >300 mg/gm creatinine), or microalbuminuria estimated by radioimmunoassay (i.e. microalbumin 30- 300 mg/day or random urine microalbumin/creatinine ratio of 30-300 mg/ gm creatinine).