Lecture (6)

Nephrotic Syndrome, IgA nephropathy (Berger disease)

The nephrotic syndrome refers to a clinical complex that includes

- ***Massive proteinuria***, with daily protein loss in the urine of 3.5 g or more in adults.
- ***Hypoalbuminemia***, with plasma albumin levels less than 3 g/dL.
- ***Generalized edema***, the most obvious clinical manifestation
- ***Hyperlipidemia*** *and* ***lipiduria***.

The nephrotic syndrome has diverse causes that share a common pathophysiology (Table 1). In all there is a derangement in the capillary walls of the glomeruli that results in increased permeability to plasma proteins. Any increased permeability resulting from either structural or physicochemical alterations in the GBM allows protein to escape from the plasma into the glomerular filtrate.

Table (1) Causes of Nephrotic Syndrome

Cause	Prevalence (100%)	
	Children	Adult
Primary Glomerular Disease		
Membranous nephropathy	*5*	30
Minimal-change disease	*65*	10
Focal segmental glomerulosclerosis	10	35
Membranoproliferative glomerulonephritis	10	10
IgA nephropathy and others	10	15
Systemic Diseases with Renal Manifestations		
Diabetes mellitus		
Amyloidosis		
Systemic lupus erythematosus		
Ingestion of drugs (gold, penicillamine, “street heroin”)		
Infections (malaria, syphilis, hepatitis B, HIV infection)		
Malignancy (carcinoma, melanoma)		
Miscellaneous (bee sting allergy, hereditary nephritis		

With long-standing or extremely heavy proteinuria, serum albumin is decreased, resulting in hypoalbuminemia and a drop in plasma colloid osmotic pressure

The resulting decrease in intravascular volume and renal blood flow triggers increased release of renin from renal juxtaglomerular cells. Renin in turn stimulates the angiotensin-aldosterone axis, which promotes the retention of salt and water by the kidney. This tendency is exacerbated by reductions in the cardiac secretion of natriuretic factors. In the face of continuing proteinuria, these alterations further aggravate the edema and if unchecked may lead to the development of generalized edema (termed ***anasarca***). At the onset, there is little or no **azotemia**, **hematuria**, or **hypertension**.

The genesis of the hyperlipidemia is more obscure. Pre uretic factors. In the face of continuing proteinuria, these alterations further aggravate the edema and if unchecked may lead to the development of generalized edema (termed *anasarca*). At the onset, there is little or no azotemia, hematuria, or hypertension.

The genesis of the hyperlipidemia is more obscure. Presumably, hypoalbuminemia triggers increased synthesis of lipoproteins in the liver or massive proteinuria causes loss of an inhibitor of their synthesis. There

is also abnormal transport of circulating lipid particles and impairment of peripheral breakdown of lipoproteins. The lipiduria, in turn, reflects the increased permeability of the GBM to lipoproteins.

IgA nephropathy (Berger disease)

This condition usually affects children and young adults and begins as an episode of gross hematuria that occurs within 1 or 2 days of a nonspecific upper respiratory tract infection. Typically, the hematuria lasts several days and then subsides, only to recur every few months. It may be associated with local pain. *IgA nephropathy is one of the most common causes of recurrent microscopic or gross hematuria and is the most common glomerular disease revealed by renal biopsy worldwide.*

The hallmark of the disease is the deposition of IgA in the mesangium. Some workers have considered IgA nephropathy to be a localized variant of *Henoch-Schonlein purpura,* also characterized by IgA deposition in the mesangium. In contrast with IgA nephropathy, which is purely a renal disorder, Henoch-Schonlein purpura is a systemic syndrome involving the skin (purpuric rash), gastrointestinal tract (abdominal pain), joints (arthritis), and kidneys.