Medicine

Nephrology

5th year – lecture 4

الدكتور

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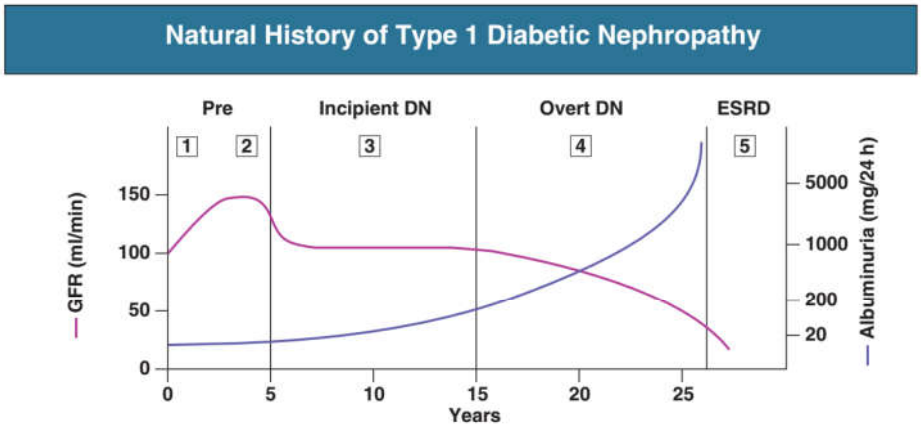
Renal involvement in systemic diseases

The kidneys may be directly involved in a number of multisystem diseases or secondarily affected by diseases of other organs.

1) **Diabetes mellitus**

Diabetes mellitus is the most common cause of CKD in developed countries. In patients with diabetes, there is a steady advance from microalbuminuria to dipstick positive proteinuria, and a progression to renal failure.

- *What is the classic diabetic glomerular lesion?*
  Kimmelstiel-Wilson nodular glomerulosclerosis (15-20%)
- *What is the more common lesion ?*
  Difuse glomerulosclerosis with a uniform increase in mesangial matrix



Stage	Pre	Incipient	Overt
Functional	GFR ↑ (25%–50%)	Microalbuminuria, hypertension	Proteinuria, nephrotic syndrome, GFR ↓
Structural	Renal hypertrophy	Mesangial expansion, GBM thickening, arteriolar hyalinosis	Mesangial nodules (Kimmelstiel-Wilson lesions) Tubulointerstitial fibrosis

Management with ACE inhibitors and other antihypertensive agents to slow progression and has been dramatically effective. Also good glycemic control, lifestyle modifcation, lipid control .

2) **Hepatic–renal disease**:

- Hepatorenal syndrome (**HRS)**: Severe hepatic dysfunction(eg cirrhosis) may cause a haemodynamically mediated type of renal failure, (hepatorenal syndrome).
  Type 1 HRS: Acute and rapid deterioration in renal function (serum creatinine ≥ 2.5 mg/dl or 220 µmol/l in less than 2 weeks) and frequently follows a precipitating event, mainly bacterial infection
  Type 2 HRS :Moderate stable renal impairment (average serum creatinine 2 mg/dl [176 µmol/l]) and mainly associated with refractory ascites
- Acute tubular necrosis: Patients with chronic liver disease are also predisposed to develop AKI (acute tubular necrosis) in response to relatively minor insults, including bleeding and infection.
- IgA nephropathy is more common in patients with liver disease.

3) **Malignancy** :

The kidney may be affected in many different ways in patients with malignant disease.

- Direct involvement of the kidneys or other parts of the urinary tract can occur, causing obstructive uropathy. (eg .uterine cancer)
- Glomerulonephritis (especially membranous nephropathy) may occur, presumably as the result of an immunological reaction to the tumour.
- Hypercalcaemia (polyuria secondary to nephrogenic diabetes insipidus and renal stones) can be caused by parathyroid hormone related protein (PTHrP) production by tumours
- Tumer lysis syndrome (usually due to hyperuricemia, diffuse tubular obstruction) : which occur during treatment of leukaemia and lymphoma
- Myeloma kidney: myeloma and other monoclonal gammopathies, renal impairment can occur as the result of the nephrotoxic effects and deposition of immunoglobulin light chains.

4) **Pulmonary-renal syndrome**:

The pulmonary–renal syndrome is a dramatic presentation with renal and respiratory failure that is not explained by excess intravascular fluid or by severe pneumonia; causes

- ❖ Diseases Associated with Antibodies to the GBM (20%-40%of cases) : Goodpasture's (antiGBM) disease .
- ❖ Diseases Associated with Systemic Vasculitis (60%-80% of cases) Granulomatosis with polyangiitis (Wegener) (common) , Microscopic polyangiitis Systemic lupus erythematosus , Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)

5) **Renal and Systemic Vasculitis** :

Small vessel vasculitis commonly affects the kidneys, with rapid and profound impairment of glomerular function. Histologically by kidney biopsy , there is a focal inflammatory glomerulonephritis, usually with focal necrosis and crescentic changes. The most important cause is antineutrophil cytoplasmic antibody (ANCA) positive vasculitis as followings :

A) **Microscopic polyangiitis (MPA)**: Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (capillaries, venules, arterioles). Necrotizing GN is common.Pulmonary capillaritis often occurs. Granulomatous inflammation is absent.

B) **Granulomatosis with polyangiitis (Wegener) (GPA)** :Necrotizing granulomatous inflammation usually involving upper and lower respiratory tract, and necrotizing vasculitis affecting predominantly small to medium vessels (capillaries, venules, arterioles, arteries, veins). Necrotizing GN is common.

C) **Eosinophilic granulomatosis with polyangiitis (Churg-Strauss) (EGPA)** : Eosinophil-rich and necrotizing granulomatous inflammation often involving the respiratory tract, and necrotizing vasculitis predominantly affecting small to medium vessels, and associated with asthma and eosinophilia.

Investigations

- Blood work: anemia (normal MCV) , increased Cr (in rapidly progressive GN), increased ESR, elevated platelet count,
- Serological testing : ANCA (**C-ANCA** with Wegener) ,(**P-ANCA** with Microscopic polyangiitis and some patients of Churg-Strauss syndrome)
- Urinalysis: proteinuria, hematuria, RBC casts
- CXR: pneumonitis, lung nodules (wegener), infltrations, cavitary lesions
- Biopsy: **renal** (segmental necrotizing glomerulonephritis), **lung** (granulomas)

Note: High level of ANCA serology and ESR often correlate with disease activity and used to monitor response to treatment in some patients

Treatment

- Prednisone 1 mg/kg/d PO ± oral or IV pulses cyclophosphamide for 3-6 months followed by azathioprine (2 mg/kg/d)
- Indications of Plasma exchange (plasmapheresis) :
  1) life-threatening pulmonary hemorrhage
  2) Patients who have dialysis-dependent renal failure at presentation.
- Consider biologic agents (as Rituximab) in refractory cases