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بالرسالة صفحات

لم ترد بالأصل

HOSSAM MAGHRABY

EVALUATION OF INTERLEUKIN-1β, INTERLEUKIN-6, TUMOUR NECROSIS FACTOR-α AND β2-MICROGLOBULIN IN CHILDREN AFFECTED WITH PRIMARY IDIOPATHIC NEPHROTIC SYNDROME

Thesis
Submitted in Partial fulfillment of M.D. Degree in Paediatrics

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بسم الله الرحمن الرحيم

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List of abbreviations

ANP: Atrial natriuretic peptide
APC: Antigen-presenting cell
α1-M: α1-microglobulin
β2-M: β2-microglobulin
ESRD: End-stage renal disease
EPO: Erythropoietin
FFA: Free fatty acids
FSGS: Focal segmental glomerulosclerosis
G-CSF: Granulocyte colony stimulating factor
GFR: Glomerular filtration rate
GM-CSF: Granulocyte-macrophage colony stimulating factor
HRP: Horseradish peroxidase
HSF: Hepatocyte stimulating factor
ICE: Interleukin-1β converting enzyme
IEF: isoelectric focusing
IFN-γ: Interferon-γ
IGF-1: Insulin-like growth factor-1
IL-1β: Interleukin-1β
IL-1Ra: Interleukin-1 receptor antagonist
IL-1RI: Interleukin-1 receptor type I
IL-6: Interleukin-6
kD: kilo dalton
LIF: Leukemia inhibitory factor
LMW: Low molecular weight proteins
MAbs: Monoclonal antibodies
MCNS: Minimal change nephrotic syndrome
MCP-1: Monocyte chemoattractant protein-1
M-CSF: Monocyte colony stimulating factor
MPGN: Membranoproliferative glomerulopathy
NAG: N-acetyl-β-D-glucosaminidase
PAF: Platelet activating factor
PDGF: Platelet derived growth factor
PGE_2: Prostaglandin E_2
RBP: Retinol binding protein
SCF: Stem cell factor
SDS-PAGE: sodium dodecyl sulfate polyacramide gel electrophoresis
TGF-β: Transforming growth factor β
TNF: Tumor necrosis factor

INTRODUCTION

INTRODUCTION

THE GLOMERULAR DISEASES

Disorders of glomerular structure and function are encountered frequently in clinical medicine. Many arise as a part of a well-defined multisystem or multi-organ disease, while in others the clinical and laboratory manifestations are consequent to the sole or predominant involvement of the glomeruli. The latter are known as the primary glomerulopathies [1].

The primary glomerular diseases are a category of glomerulonephritis in which clinical and biochemical abnormalities are the sole or predominant consequences of damage to the integrity of glomerular structure and/or function. Clinically, several syndromes are found (Table I). These syndromes arise as a result of the admixture of hematuria, proteinuria, reduced glomerular filtration rate, and sodium chloride and water retention-all these are cardinal manifestations of glomerular disease [1].

The primary glomerular diseases are best classified according to the principal clinical and laboratory manifestations of the disease. The findings in urine analyses, specifically the extent and nature of hematuria and proteinuria are extremely useful in defining glomerular diseases [2].

Many glomerulopathies are immunologically mediated. With the use of immuno-histologic techniques (immunofluorescence or immunoperoxidase), the presence or absence of antibody, antibody class, site of deposition (capillary wall or mesangium), and patterns of deposition (granular or linear) can be determined [2].

Linear capillary wall deposition is usually indicative of the presence of an autoantibody (most often IgG) directed against intrinsic glomerular

basement membrane antigens. In most cases, the antigenic site lies within a non-collagenous domain of the α3 domain of type IV collagen [1].

Granular patterns of immunoglobulin deposition and electron dense deposits are indicative of immune complex presence in the glomeruli. The antigen may be endogenous (e.g. nuclear antigens or histones), or exogenous (e.g. viral or bacterial antigens). The antigen may also be intrinsic or extrinsic to the kidney (renal or non renal endogenous antigens). Circulating immune complexes composed of extrinsic (non-renal) antigens and antibody may be deposited in the glomeruli. Some antigens normally extrinsic to the glomeruli may localize within glomerular structures and form immune complexes *in situ* by reacting with circulating antibodies [2].

Polyangiitis is a situation in which autoantibodies against neutrophil cytoplasmic antigens are formed [1].

Table (I): Clinical presentations of glomerular diseases [3].

Category	Common diseases which manifest this syndrome
Asymptomatic proteinuria	Focal segmental glomerulosclerosis. Mesangioproliferative glomerulonephritis.
Nephrotic syndrome	Minimal change glomerulopathy. Membranous glomerulopathy. Focal segmental glomerulosclerosis. Mesangioproliferative glomerulonephritis. Membranoproliferative glomerulonephritis. Diabetic glomerulosclerosis. Amyloidosis Light chain deposition disease Fibrillary glomerulonephritis
Asymptomatic microscopic hematuria	Thin basement membrane nephropathy. IgA nephropathy. Mesangioproliferative glomerulonephritis. Alport's syndrome.
Recurrent gross hematuria	Thin basement membrane nephropathy. IgA nephropathy. Alport's syndrome
Acute glomerulonephritis	Acute diffuse proliferative glomerulonephritis. Post streptococcal glomerulonephritis. Membranoproliferative glomerulonephritis.
Focal proliferative glomerulonephritis	IgA nephropathy
Rapidly progressive glomerulonephritis	Crescentic anti-GBM glomerulonephritis. Crescentic immune complex glomerulonephritis. Crescentic antineutrophil cytoplasmic autoantibodies glomerulonephritis
Nephritis with systemic vasculitis	Goodpasture's syndrome. Immune complex vasculitis: Henoch-Schonlein purpura Cryoglobulinemia Antineutrophil cytoplasmic autoantibodies vasculitis: Microscopic polyangiitis. Wegner's granulomatosis. Churg-strauss syndrome.
Chronic glomerulonephritis	Chronic sclerosing glomerulonephritis

REVIEW OF LITERATURE