Management of Membranous Nephropathy

An essay submitted for partial fulfillment of the master degree in Internal Medicine

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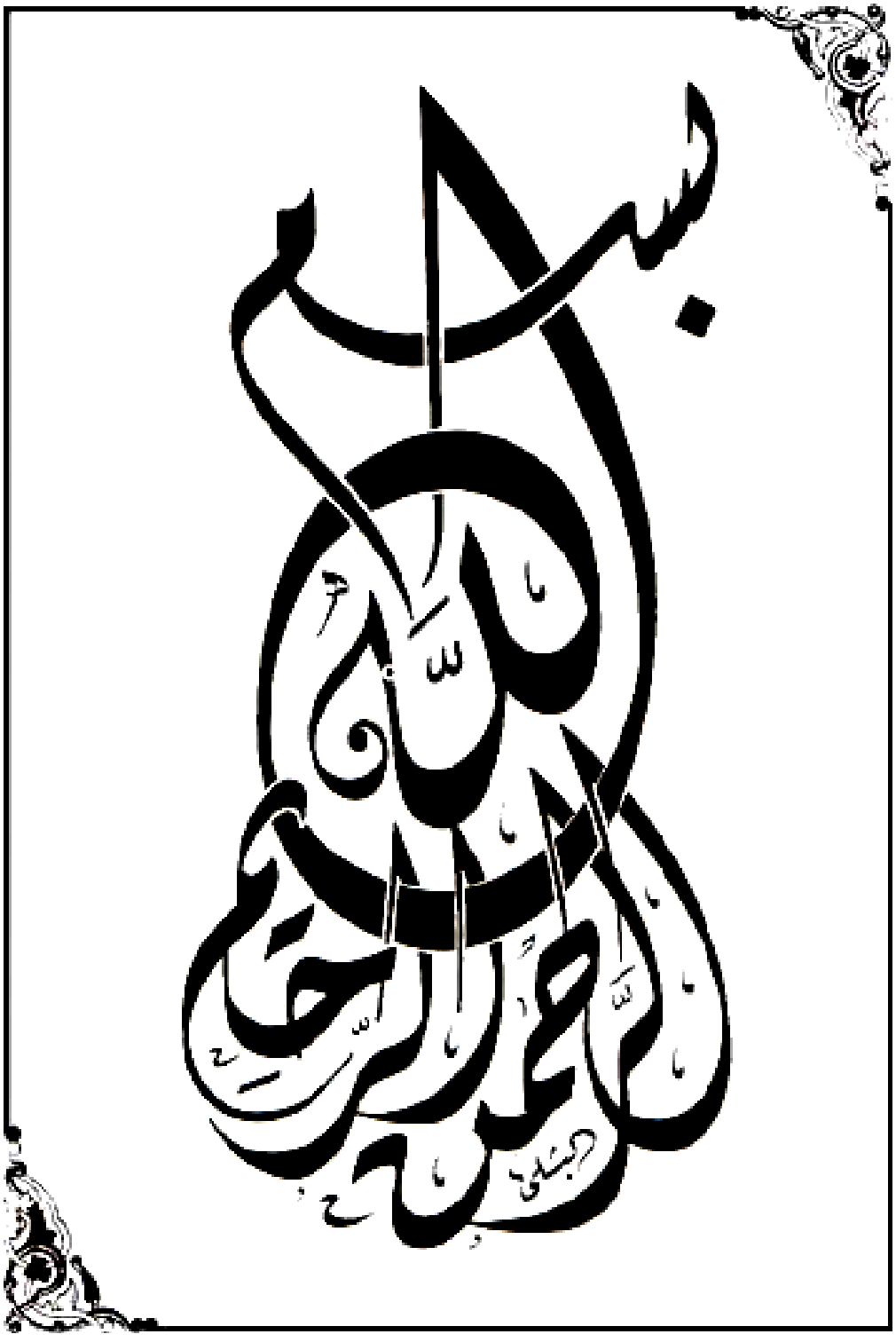
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List of Abbreviations :

- **ACEi** : Angiotensen Converting Enzyme inhibitors
- **ACTH** : Corticotropin
- **ANCA** : Antineutrophil cytoplasmic antibody.
- **ARBs** : Angiotensen Receptor Blockers.
- **CR** : Complete Remission.
- **CR1** Membrane complement receptor 1.
- **CRP** : Complement Regulatory Protein.
- **CsA** : Cyclosporine A.
- **ECC** : Effective creatinine clearance
- **ESRD** : End Stage Renal Disease.
- **FGS** : Focal Glomerulonephritis.
- **GBM** : Glomerular Basement Membrane.
- **GFB** : Glomerular Filtration Barrier.
- **GFR** : Glomerular Filtration Rate.
- **HBV** : Hepatitis B Virus.
- **HCV** : Hepatitis C Virus.
- **HEV** : Hepatitis E Virus.
- **HIV :** Human Immunodeficiency Virus**.**
- **HLA** : Human Leukocyte Antigen.
- **HN** : Heymann Nephritis
- **IMGN** : Idiopathic Membranous Glomerulonephritis.
- **Kf** : The two Kidney ultrafiltration Co-efficiency.
- **MAC**: Membrane Attack Complex.
- **MCD**: Minimal Change Disease.
- **MGN**: Membranous Glomerulonephritis
- **MLN**: Membranous Lupus Nephritis
- **MMF**: Mycophenolate Mofetile.
- **MN** : Membranous Nephropathy.
- **MTP:** Methyl prednisolone
- **NEP**: Neutral Endopeptidase.
- **NG**: Total number of functioning Glomeruli**.**
- **NS**: Nephrotic Syndrome.
- **NSAID:** Non Steroidal Antiinflammtory Drugs**.**

- **OTC** : Over the- counter- preparations
- **PDGF-B**: Podocyte Growth Factor-B.
- **PDGF-C**: Podocyte Growth Factor-C.
- **PR**: Partial Remission.
- **RFD**: Renal Function Deterioration.
- **ROS** : Reactive Oxygen Species.
- **Screat**: Serum Creatinine.
- **SLE** : Systemic Lupus Erythrematosis.
- **SPARC**: Secreted Protein Acidic and Rich in Cysteine.
- **Tac :** Tacrolimus
- **TGF-B**: Tumor Growth Factor –B.
- **TMP-SMX** : Trimethoprim-Sulfamethoxazole.
- **VEGF**: Vascular Endothelial Growth Factor.

Introduction

Introduction

Membranous nephropathy is the most frequent cause of idiopathic nephrotic syndrome in adults. **(Haas et al, 1997)**

MGN is characterized by basement membrane thickening and subepithelial immune deposits without cellular proliferation or infiltration. **(Burstein et al, 1993)**

MGN is a classic instance of immune complex deposition disease and complement activation. **(Farquhar et al,1995)**

Membranous nephropathy can be idiopathic or secondary (30%) .The two can be distinguished by clinical, laboratory, and histological features. **(Haas et al, 1997)**

The clinical course of membranous nephropathy is usually benign or indolent but 30-40 % of patients progress toward end stage renal failure within 5 to 15 years. **(Honkanen et al, 1992 & Reichert et al, 1998)**

Several therapeutic approaches have been tried in patients with membranous nephropathy, Corticosteroids have been largely used but a meta analysis of the available controlled trials didn't show any benefit of corticosteroids either in favoring remission of the nephrotic syndrome or in preventing renal dysfunction and controversial results have been obtained with cytotoxic agents . **(Hogan et al, 1995)**

The treatment of idiopathic membranous nephropathy (IMN) remains a controversial issue . Over the past 30 years many different regimens have been recommended for the treatment of IMN, however, the attempts to define the optimal management of IMN have been substantially hampered by the extremely variable course of the disease. **(Muirhead N, 1999 & Schieppati et al ,2004)**

Despite extensive clinical investigations in the past two decades,the injury is still out on optimal scheme of management of this type of glomerulonephritis, in particular the efficacy and safety of majority of protocols employing corticosteroids and alkylating agents must be regarded at least controversial . **(Ruggenenti et al, 2003)**

Treatment with alkylating agents is associated with an increased rate of remission in patients with nephrotic syndrome and idiopathic membranous nephropathy when compared to steroid therapy alone or no therapy. **(Schieppati et al, 2004 & Merlin Thomas, 2005)**

There is no data to support the short term use of steroids on their own for the treatment of patient with nephrotic syndrome and idiopathic membranous glomerulonephropathy. **(Yokoyama et al, 2004 & Merlin Thomas, 2005)**

Aim of the work:

To review literature about the subject of Membranous Nephropathy and to conclude a scheme for management of Membranous Nephropathy .

Chapter 1

Membranous Nephropathy

Epidemiology :

The disease affects patients of all ages and races.MGN is idiopathic in the majority of cases, approximately 25% of adults and 80% of children have an identifiable immunological stimulus. **(Yoshikawa et al, 1985)**

The incidence of secondary forms may be influenced by the prevalence of hepatitis or malaria in certain areas. **(Sabe et al, 1986)**

Idiopathic disease has a male and adult predominance with a male – to –female ratio of 2: 1. **(Harrison et al, 1986)**

The peak incidence is between 30 and50 years, and MGN is particularly likely in patients over 50 yr of age who present with nephrotic syndrome. Onset outside the usual range is more likely to be a result of secondary causes. **(Yokoyama et al, 2004)**

Mortality / Morbidity .

The course is variable and patients may be divided into 3 groups of approximately equal size (ie," rule of thirds") .
Patient in the first and second category die from non renal causes.

* Spontaneous complete remission. Renal function is normal , with or without subsequent relapse .
* Persistent proteinuria of variable degree; Renal function is normal or impaired but stable.
* Progressive disease , eventually leading to end – stage renal disease (ESRD).

The incidence rate of ESRD is 14% at 5 years, 35% at 10 years , and 41% at 15 years. **(Reichert et al, 1998)**

Pathology :

The hallmark of MGN is subepithelial deposition of immunoglobulin G (IgG) together with (in idiopathic MGN)

normal cellularity of the glomerular tuft .

A- Light microscopy :

The mesangium is normal, with no hypercellularity. All glomeruli are involved . The capillary walls are thickened with patent capillary lumina . Subepithelial deposits are seen : with trichrome stain , they are shown to have spikes . **(Figure 1**)

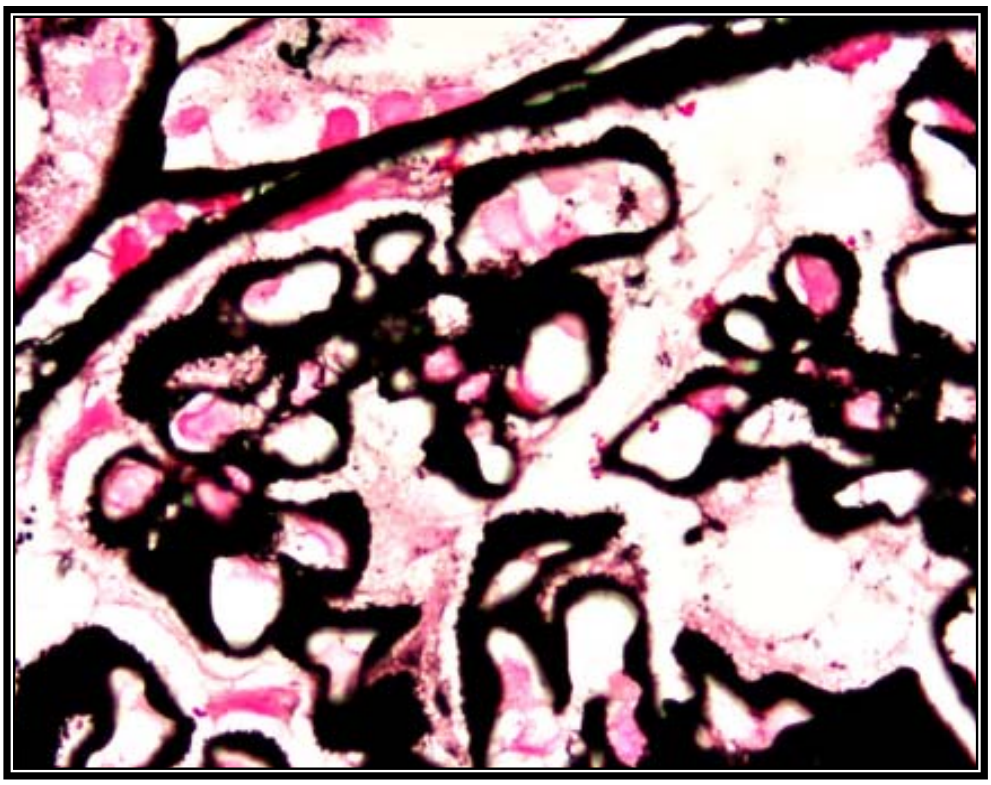

Figure (1) : Thickened glomerular basement in MGN