





MEMBRANOUS GLOMERULONEPHRITIS

Focus on tissue and serum Anti-Phospholipase A2 receptor (PLA2R) antibody testing

Compiled by Dr Julian Deonarain

3rd Quarter 2019

Introduction

Membranous glomerulonephritis (MGN) is a common cause of adult nephrotic syndrome (NS). MGN is characterised by glomerular basement membrane thickening (Figure 1A) with glomerular immune complex deposition. Immune complex deposition may be demonstrated as granular deposits on immunofluorescence (Figure 1B) or sub-epithelial deposits on electron microscopy (Figure 1C).



Figure 1. Membranous glomerulonephritis

MGN can be classified as either primary or secondary, based on the identification of an underlying disease.

Secondary MGN

Diseases associated with secondary MGN include:

- · Auto-immune diseases: Systemic lupus erythematosus, Sjögren's syndrome, Sarcoidosis
- Malignancy: Carcinoma, Lymphoma
- Infections: Hepatitis B, Hepatitis C, Syphilis, HIV
- Drugs: NSAIDs, Gold, Penicillamine

Primary MGN

Primary membranous glomerulonephritis does not have a known disease association. Research has uncovered the target glomerular antigens, which can be summarised as follows:

- Phospholipase A2 receptor (PLA2R)
 - Expressed on podocytes and proximal tubules
 - o IgG4 anti-PLA2R antibodies are detected in approximately 70% of primary MGN cases
- Thrombospondin type 1 domain-containing 7A
- Detected in 2.5% 5% of primary MGN cases
- Membrane metallo-endopeptidase/neutral endopeptidase/CD10
 - Rare neonatal form of MGN
 - 1st human antigenic target of MGN identified
- Aldose reductase (AR) and manganese superoxide dismutase 2 (SOD2)

Anti-PLA2R antibody testing available at Lancet Laboratories

- Serum anti-PLA2R antibody testing
 - Elevated in approximately 70% of idiopathic MGN cases.
 - Raised levels are also reported in patients with disease-specific secondary MGN sarcoidosis (64%), ANCA kidney disease (16%), Sjögren's disease (16%), Hepatitis B virus (11%), and Hepatitis C virus (65%).
 - Antibody testing has been incorporated into diagnostic and investigative algorithms for nephrotic syndrome.
 - o It provides prognostic information about disease severity and monitoring treatment.
 - Spontaneous remission is more common in patients with low antibody levels.
 - Patients with high antibody levels show lower immunosuppressive therapy responses and a longer time to remission.
 - The relapse rate correlates with the antibody level at the time of clinical remission.
 - High antibody levels are associated with a high risk of progressive kidney failure.

- Immunohistochemistry to detect anti-PLA2R tissue deposition
 - Undertaken on formalin-fixed paraffin embedded renal biopsies routinely submitted for light microscopy.
 - Normal weak expression in resident podocytes (Figure 2A).
 - Idiopathic MGN shows diffuse strong capillary loop expression, which corresponds to anti-PLA2R autoantibody deposition (Figure 2B).



Figure 2. Immunohistochemistry to detect anti-PLA2R tissue deposition

References

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Johannesburg	g (011) 358 0800	Polokwane	e (015) 294 0400	Cape Town (02	21) 673 1700	Welkom (0)57) 355 9003
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