LABUPDATE no. 45

October 2023

THE ANTI-PLA2 RECEPTOR ANTIBODIES TEST

Membranous nephropathy (MN) is characterised by a thickening of the glomerular capillary walls due to immune complexes that are formed on the outer surface of the basement membrane. MN is the most common cause of nephrotic syndrome in adults without underlying diabetes mellitus.

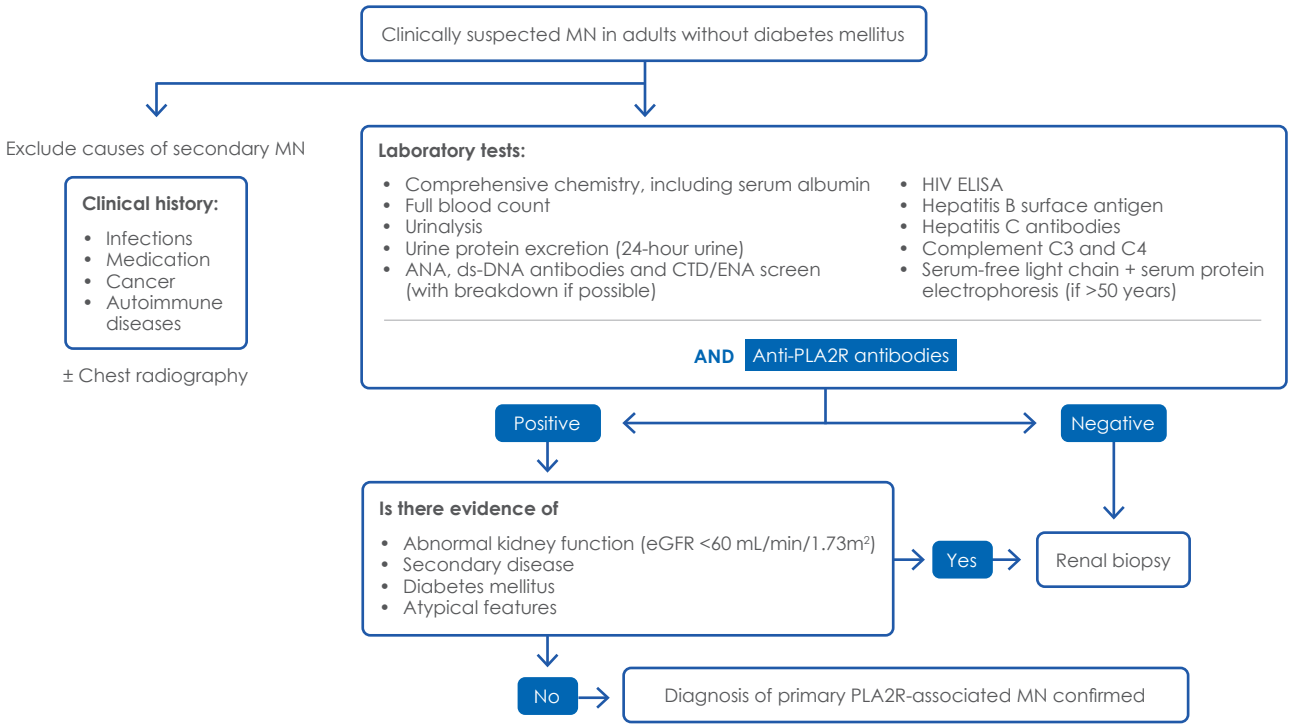
Approximately 20% of MN cases are caused by conditions such as autoimmune diseases, hepatitis B or C virus infections, thyroiditis, malignancies or medication use, for example non-steroidal anti-inflammatory drugs (NSAIDs). The remaining 80% are deemed primary membranous nephropathy (PMN), with no identifiable cause. It has been demonstrated that up to 80% of patients with PMN have auto-antibodies against the podocyte antigen phospholipase A2 receptor (PLA2R). Progressive auto-antibody binding to the podocyte and immune deposits (complexes) eventually leads to injury and impaired filtration. Anti-PLA2R antibodies are considered highly specific for PMN.

The diagnosis of MN should be considered in all adult patients who present clinically with nephrotic syndrome (including features such as proteinuria, hypoalbuminemia, edema and weight gain).

DIAGNOSTIC APPROACH TO MEMBRANOUS NEPHROPATHY (MN)

The Kidney Disease: Improving Global Outcomes (KDIGO) 2021 guidelines on the management of glomerular disease recommend a non-invasive approach to the diagnosis of PMN in adults with nephrotic syndrome, primarily through the incorporation of anti-PLA2R antibody testing. Figure 1 outlines the recommended approach to the diagnosis of clinically suspected MN.

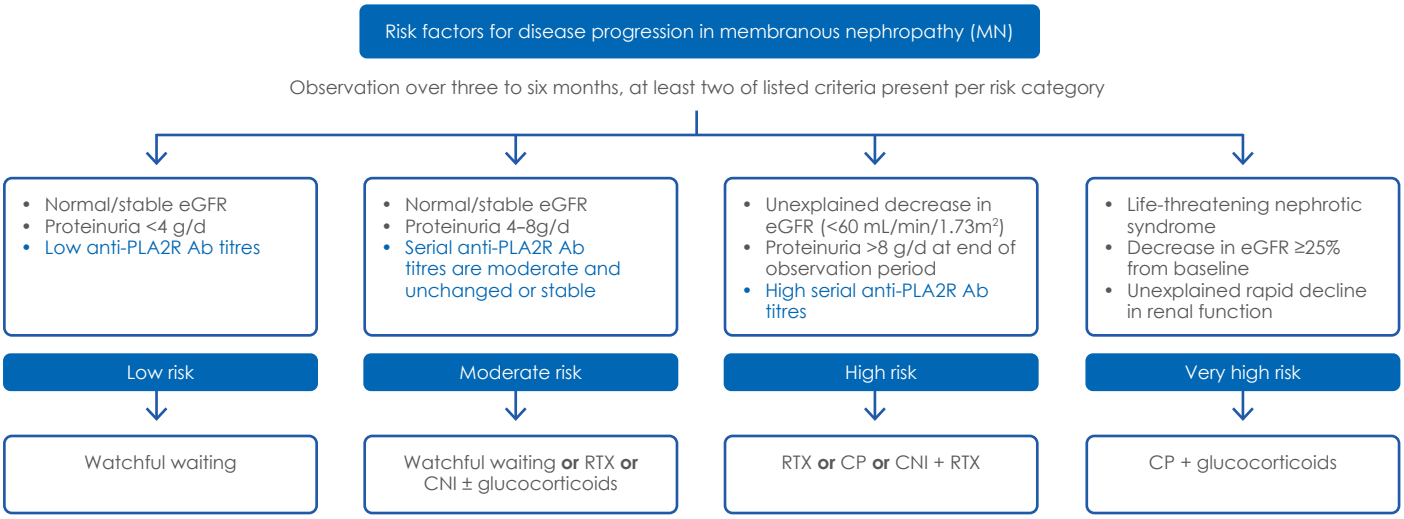
FIGURE 1: DIAGNOSTIC APPROACH TO MEMBRANOUS NEPHROPATHY (MN)



ROLE OF ANTI-PLA2R ANTIBODIES IN MONITORING OF PMN

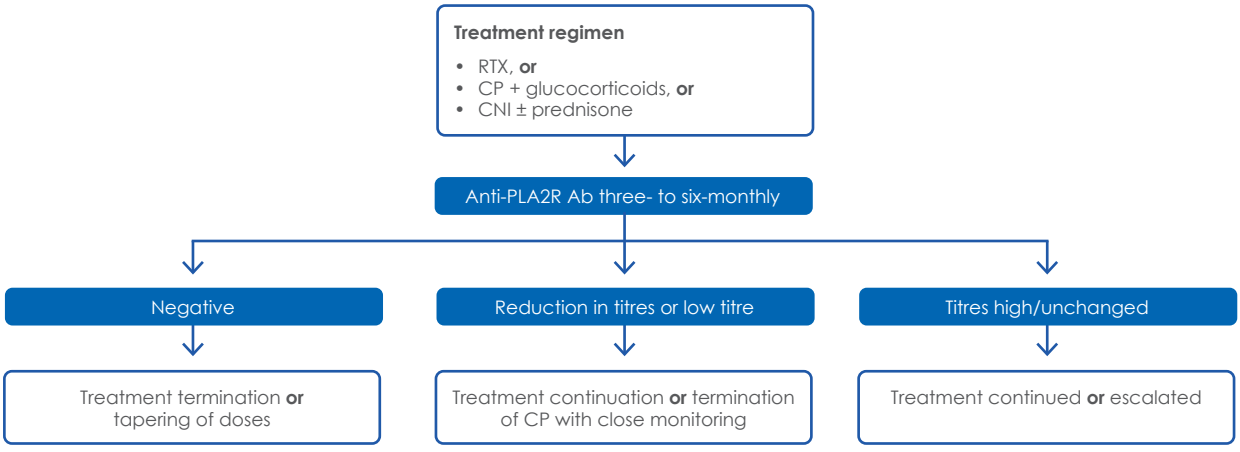
Changes in the anti-PLA2R antibody titres have been shown to precede a change in the clinical status of patients with PMN, with a high predictive value for clinical outcome and risk assessment. Serial assessment of anti-PLA2R antibody titers can be applied, together with other parameters, to predict the risk of disease progression (see Figure 2). The trends in anti-PLA2R antibody titres may also give an indication of the immunological response to treatment, which should be considered alongside other parameters, such as 24-hour urine protein excretion, serum creatinine and serum albumin (see Figure 3). The KDIGO guidelines also recommend that anti-PLA2R antibodies be checked prior to renal transplantation, owing to an increased risk of disease recurrence associated with high anti-PLA2R antibody titres.

FIGURE 2: RISK FACTORS FOR DISEASE PROGRESSION IN MN



Ab: Antibody; CNI: Calcineurin inhibitors; RTX: Rituximab; CP: Cyclophosphamide-based protocol

FIGURE 3: IMMUNOLOGICAL MONITORING OF TREATMENT FOR MN



CNI: Calcineurin inhibitors; RTX: Rituximab; CP: Cyclophosphamide-based protocol

TABLE 1: ANTI-PLA2R ANTIBODIES TEST INFORMATION

Method	Transfected cell-based indirect immunofluorescence (IIFT)
Specimen type	Serum (SST tube)
Turnaround time*	48 hours (performed on weekdays only)
Test mnemonic	**PLA2R**
Test characteristics	Sensitive and highly specific assay to support the diagnosis of PMN. Advantages of the IIFT method include being a cost-conscious test option, and no requirement for batch testing results in improved turnaround time.

*Once received at the National Reference Laboratory.

REFERENCES AVAILABLE ON REQUEST