THE PATHCARE NEWS

PRECISION ANTI-PLA2R QUANTIFICATION FOR MEMBRANOUS NEPHROPATHY

Membranous Nephropathy (MN) is among the most common causes of nephrotic syndrome in adults without diabetes. If left untreated, it can progress to kidney failure. Depending on the absence or presence of associated conditions, MN is traditionally classified as primary ("idiopathic") or secondary. **Secondary MN** (sMN) is related to underlying conditions such as malignancies, infections (e.g., hepatitis B or C), certain medications, or autoimmune conditions (e.g., systemic lupus erythematosus). **Primary MN** (pMN) accounts for 70-80% of MN cases and is characterized by immune complex deposits at the glomerular basement membrane, leading to damage to the filtration barrier and subsequent proteinuria. **Recent studies have shown that in approximately 70% of patients with primary MN, the immune complexes consist of autoantibodies against the podocyte protein M-type phospholipase A2-Receptor (PLA2R). This discovery has improved diagnostic laboratory accuracy and guided therapeutic approaches.**

The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, updated in 2021, recommend using anti-PLA2R antibody testing as part of the diagnostic workup for patients with suspected pMN. The levels of anti-PLAR2 antibodies have been shown to correlate with disease activity in pMN; higher levels are generally associated with more active disease and a worse prognosis. Monitoring anti-PLA2R levels can provide valuable insights into disease progression and response to treatment.

In alignment with the KDIGO guidelines, **PathCare now offers the PLA2R indirect immunofluorescence assay (IFA) with quantification of positive cases using the PLA2R ELISA method. This dual approach allows for precise quantitative monitoring of the disease activity, enhancing the ability to tailor treatment strategies effectively.**

Screening/Diagnosis – Anti-PLA2R by IFA Method

→ **PLA2R IFA NEGATIVE at titre 1:10**

A negative serological test for PLA2R does not exclude the diagnosis of MN. Approximately 20-30% of cases may test negative early in the disease course, or the MN may be related to other target antigens besides PLA2R. In such cases, a kidney biopsy may be necessary to confirm diagnosis.

→ **PLA2R IFA POSITIVE at titre 1:10**

A positive PLA2R on the IFA test method will be followed by quantification using the ELISA method. A positive IFA result, combined with an ELISA result ≥ 2 RU/mL, is considered as confirmatory for the presence of anti-PLA2R antibodies (Refer to study by Bobart SA et al).

Request test: J6154 ☑ **PLA2-R Screening**

Monitoring – Anti-PLA2R by Quantitative ELISA Method

Once a baseline value for PLA2R has been established at diagnosis, the disease activity can be monitored using the quantitative ELISA method. The KDIGO guidelines recommends monitoring levels every 3 - 6 months, with more frequent monitoring advised for high-risk patients to guide treatment decisions.

PLA2R (Quantitative ELISA):

< 2 RU/mL:	Considered seronegative
>50 RU/mL:	High risk for disease progression
>150 RU/mL:	More frequent monitoring indicated.

While the PLA2R ELISA assay is slightly less sensitive than the IFA method, both methods have equal specificities. The ELISA assay is valuable for ongoing monitoring, determining the risk of disease progression, assessing response to immunosuppressive therapy, and predicting relapse following kidney transplantation.

Request test: Z6155 ☑ **PLA2-R (ELISA Quant) Monitoring**

Conclusion:

The availability of the PLA2R IFA, with its higher sensitivity, is essential for initial screening to detect the presence of PLA2R antibodies. A positive IFA result strongly suggests the presence of pMN and should be followed by the quantitative ELISA method. This sequential approach allows for precise quantification of PLA2R antibody levels, which is critical for ongoing monitoring, assessing the risk of disease progression, and guiding treatment decisions.

References:

1. Beck LH Jr et al. M-type phospholipase A2 receptor as target antigen in idiopathic membranous nephropathy. N Eng J Med 2009; 361:11-21.
2. KDIGO 2021 Clinical practice guideline for the management of glomerular diseases. Kidney Int 2021; 100(4S):S1-S276.
3. Bobart SA, De Vriese AS, Pawar AS, et al. Noninvasive diagnosis of primary membranous nephropathy using phospholipase A2 receptor antibodies. Kidney Int. 2019;95(2): 429-438.Ref: Saschenberger S et al. Serological diagnosis of autoimmune bullous skin diseases. Frontiers Immunol 2019; 10(1974).

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