**Introduction**

Membranous Nephropathy is the leading cause of nephrotic syndrome in adults. In about 25% of patients, Membranous Nephropathy is associated with a secondary cause such as SLE and malignancy. When no etiology is identified, it is classified as Primary Membranous Nephropathy. However, membranous nephropathy can also appear months before a secondary cause is identified. Herein, we report the case of a patient diagnosed with Membranous Nephropathy later found to be secondary which was associated with positive Phospholipase A2 Receptor antibodies.

**Case Description**

A 70-year old male was initially referred to us for evaluation of worsening lower extremity edema. He had a known history of Chronic Kidney Disease Stage II that was thought to be secondary to Diabetes. He had recently been admitted to the hospital where he was found to have proteinuria in excess of 7 grams over 24 hours. Differential Diagnosis included Primary Nephrotic Syndrome which included Minimal Change Disease and Membranous Nephropathy. Consequently, a CT-guided Renal Biopsy was ordered.

Renal Biopsy showed evidence of focal tubular atrophy along with granular deposition of Immunoglobulin G and C3. The glomerular capillaries showed sub-epithelial electron dense deposits along with foot process effacement. Findings were hence, suggestive of membranous glomerulonephritis superimposed on modest arterionephrosclerosis. To evaluate for malignancy related membranous nephropathy, cancer-screening was ordered. CT Scan of the Chest did not show any evidence of malignancy. Due to an elevated Creatinine, a CT Scan of the Abdomen was ordered but not completed. Antiphospholipase A2 Receptor antibodies by IFA and ELISA were also sent. The IFA titer was noted to be 1:500 and was 186.00 RU/mL by ELISA. Primary Membranous Nephropathy was suspected and the patient was started on the Ponticelli Regimen. About 4 months later, the CT Scan of the Abdomen revealed the presence of a Pancreatic Adenocarcinoma. The presence of a Pancreatic Malignancy could be co-incident with the finding of Primary Membranous Nephropathy, or could represent Secondary Membranous Nephropathy with a positive Anti-phospholipase A2 Receptor Antibody.

**Pathological Analysis**

Subepithelial electron dense deposits partially surrounded by Glomerular Basement Membrane with epithelial cell foot process effacement. Consistent with membranous Glomerulonephritis.

Fine granular deposits of IgG and C3 are present in glomerular capillary loops.

Trichome loops with thickened loops and no proliferation. Silver Stain shows epimembranous spikes (arrow).

**Discussion**

Membranous Nephropathy is one of the leading causes of Nephrotic Syndrome in the adult population. It is characterized by the formation of sub-epithelial immune complexes that damage the glomerulus. Primary Membranous Nephropathy is characterized by circulating autoantibodies binding to antigens located on the surface of podocytes. In about 20% of cases, membranous nephropathy may be secondary to various disorders including systemic diseases (SLE and sarcoidosis), infections (hepatitis B), drugs and malignancy. 2

Antigenic targets implicated in Primary Membranous Nephropathy include M-type Phospholipase A2 Receptor (75%) and Thrombospondin Type-1 Domain Containing 7A Antigen (5%). Levels of the above antibodies have been found to co-relate with both severity and prognosis of the disease. 2,3 Autoantibodies against PLA2R are both sensitive and specific (about 70%) for Primary Membranous Nephropathy. However, these antibodies have been detected in some cases of Secondary Membranous Nephropathy as well. 4,5 Whether this is a co-incident finding or related to the pathogenesis of Secondary Membranous Nephropathy remains unclear. 1 As in our case, the presence of PLA2R autoantibodies may suggest the presence of Primary Membranous Nephropathy in conjunction with malignancy or maybe a different autoimmune process altogether. Using a combined approach of testing for both PLA2R autoantibodies and malignancy may have been useful as it was found to increase the sensitivity of detection from 77.8 to 89.6%. 4,6

As noted in our case, the presence of autoantibodies still poses a clinical dilemma with regards to the classification of Membranous Nephropathy. As demonstrated by previous studies, the presence of autoantibodies cannot effectively rule out the presence of a secondary etiology.

**Conclusion**

We strongly believe that more clinical studies will be needed in the upcoming future to help us clearly establish a distinction between Primary and Secondary Membranous Nephropathy.

**References**