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# Interesting Case Of Membranous Nephropathy – Indigenous Medicine Induced

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## Abstract

**Background:** Membranous Nephropathy (MN) is a progressive kidney disease which is characterized by the accumulation of immune complexes within the kidney that can occur at all ages. Here we present a 65 year old female patient presented with history of puffiness of face and decreased urine output since 4 days. With preliminary findings a diagnosis of Nephrotic Syndrome with Renal failure was made and further evaluated for Renal biopsy. Jones Methamine Silver Staining showing Perpendicular projections in the outer aspect of Glomerular basement membrane adjacent to deposits. Renal biopsy showed Grade II Membranous Nephropathy (Ehrenreich & Churgh Classification) & tissue staining for Phospholipase A2 Receptor antibody (PLA2R) was negative. With the above findings and history of indigenous medication consumption, a diagnosis of Membranous Nephropathy secondary to intake of Indigenous medicines was made.

**Conclusion:** Since PLA2R was negative and patient gave history of indigenous medicine intake, we conclude that this is probably a case of Membranous Nephropathy secondary to intake of indigenous medicines.

**Keywords**: Nephrotic Syndrome, Membranous Nephropathy, Indigenous Medicines, Kidney.

## Introduction

Membranous Nephropathy (MN) is a progressive kidney disease which is characterized by the accumulation of immune complexes within the Kidney that can occur at all ages.[1] It can either be Primary or Secondary. Primary form is an autoimmune disease caused by autoantibodies directed against Phospholipase A2 receptor (PLA2R). Secondary causes includes infections, drugs, malignancy and other autoimmune diseases. Drug induced MN is due to the immune response to the drugs or to a by-product that act as planted antigen on a subepithelial position of the GBM. It is a glomerular disease that occur in all ages with mean age of diagnosis at 50-60 years.[1] It may be Primary MN (75%) or Secondary MN which is associated with medications or toxins, autoimmune diseases such as Systemic Lupus Erythematosus, Rheumatoid Arthritis, Sjogren's syndrome, Infections like Hepatitis B virus, Hepatitis C virus, HIV & Malignancies like Lung carcinoma, Gastric Carcinoma.[2]

Clinically, the majority of patients have nephrotic syndrome or proteinuria diagnosed on a routine urinalysis. Idiopathic MN affects people of all ages, ethnicities, and sexes all over the world, and it is the primary cause of nephrotic syndrome in Caucasian adults. Although spontaneous remission of the condition is more prevalent in children, it can also occur in adults.[3–6] Here, we are reporting a case of Nephrotic Syndrome diagnosed as Membranous Nephropathy secondary to Indigenous medicine intake.

**Case Details**

A 65 year old lady with a history of hypothyroidism for 5 years and systemic hypertension for 1 year presented with the complaints of puffiness of face and decreased urine output of 4 days duration. She gives history of taking indigenous medicines for Osteoarthritis for the past 2 months. On Examination, her Vitals were stable, Systemic Examination were normal there is no evidence of hypertensive retinopathy. We proceeded with the Routine investigation which is shown in table :

**Table 1: Blood investigations report of the patient**

| **INVESTIGATIONS** | **DAY 1** |
|---|---|
| Hemoglobin | 10.9 g/dl |
| Total WBC counts | 8600 cells/$mm^3$ |
| Platelets | 3.29 L /$mm^3$ |
| SGOT | 20 U/L |
| SGPT | 24 U/L |
| Urine Albumin<br>Urine Sugar | 3+<br>Nil |
| FBS<br>PPBS<br>HbA1C | 84 mg/dl<br>110mg/dl<br>6 % |
| Total Cholesterol<br>Triglycerides | 150 mg/dl<br>86 mg/dl |
| Hepatitis B<br>Hepatitis C<br>HIV I & II | Non Reactive |
| Chest X ray | Normal |
| ECG | Normal Sinus Rhythm |
| ECHOCARDIOGRAM | Normal |
| Stool Occult Blood | Negative |
| Mammogram | Normal |
| RA Factor | Negative |
| ANA Profile | Negative |



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| **Table 2: Follow-up details of the patients** | | | |
|---|---|---|---|
| **Investigations** | **Day 1** | **Day 5** | **day 10** |
| Urea | 44 mg/dl | 55 mg/dl | 34 mg/dl |
| Creatinine | 2 mg/dl | 1.7 mg/dl | 1.2 mg/dl |
| Serum Albumin | 1.9 mg/dl | | 3.0 mg/dl |
| 24 Hour Urine Protein | 4983 mg/dl | | 3500 mg/dl |

With the preliminary report, 24 hour urine protein was 4983mg/dl & Serum Creatinine was 2 mg/dl. USG Abdomen showed no significant abnormality. With considering all the findings a diagnosis of Nephrotic Syndrome with Renal failure and proceeded further with Renal biopsy was made initially.

**Light microscopy**

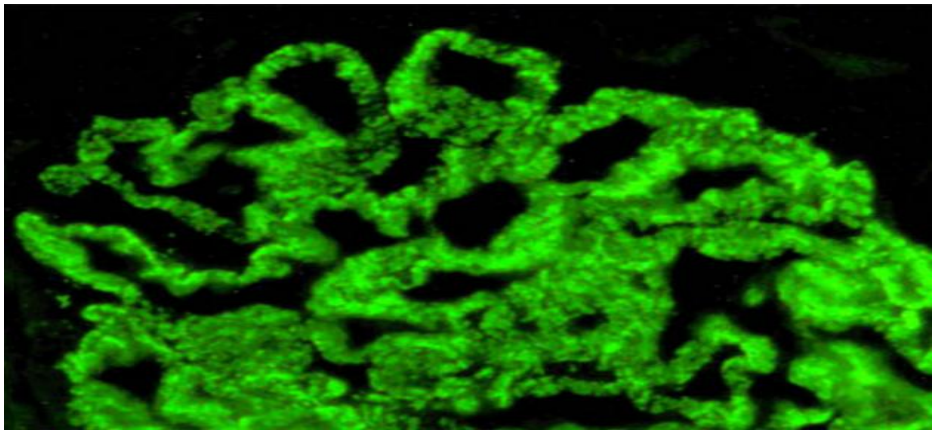
Jones Methamine Silver Staining showing Perpendicular projections in the outer aspect of Glomerular basement membrane adjacent to deposits.

**Immunofluorescence**

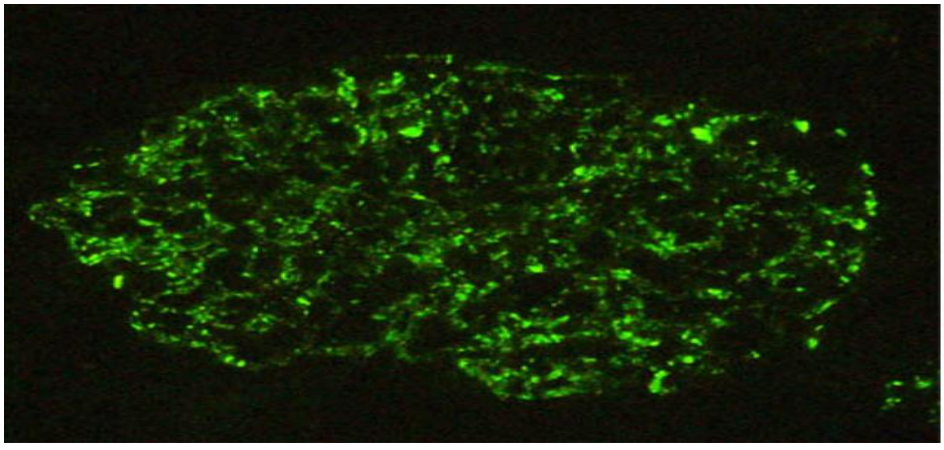
Granular positivity on the capillary loops. [A] IgG(+3) and [B] C3(+1)

**Figure 1: Immunofluorescence showing Granular positivity on the capillary loops. [A] IgG (+3) and [B]C3 (+1)**

a)



b)





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**Tissue staining for PLA2R antibody**

**[a] PLA2R - Negative**

Renal biopsy showed Grade II Membranous Nephropathy (Ehrenreich & Churgh Classification) & Tissue staining for Phospholipase A2 Receptor antibody was Negative. There was no evidence of underlying malignancy. Antinuclear antibody testing and serologic testing for Hepatitis B, Hepatitis C and HIV was turned out to be negative. Her baseline blood investigations which was done 3 months back were within normal limits. Since PLA2R was negative & patient gave history of taking indigenous medicines, we came to the conclusion that this is probably a case of Membranous Nephropathy secondary to intake of Indigenous medicines. After admission, Patient abstained from the use of indigenous medicine & she was started on Diuretics, Angiotensin Receptor Blockers, Angiotensin Converting Enzyme inhibitors. Patient got symptomatically improved and discharged with stable vitals. During 3 month follow up, Patient reviewed with Urine PCR of less than 0.3, Serum Creatinine of 1.

## Discussion

Membranous Nephropathy is the leading cause of Nephrotic Syndrome in adults. Autoantibodies directed against phospholipase A2 receptor antigen, thrombospondin type 1 domain-containing 7A, and neural epidermal growth factor-like 1 protein cause primary MN.[2] MN, on the other hand, can be caused by a number of secondary causes, including but not limited to autoimmune illnesses, malignancies, infections, and drug and heavy metal exposure, including gold and mercury.[7]

Membranous Nephropathy is a disease which is characterized by basement membrane thickening with minimal or no cellular proliferation and the presence of immune deposits like IgG on the epithelial side of the glomerular capillary wall.[8] MN is defined by a pathological alteration in the glomerular basement membrane (GBM) produced by immune complex accumulation, which appears as granular immunoglobulin (Ig)G deposits when photographed with immunofluorescence and as electron-dense deposits when scanned with electron microscopy. The complement membrane assault complex is seen in these immunological deposits between podocytes and GBM (C5b-9). MN can be idiopathic (idiopathic membranous nephropathy, or IMN) or partially caused by clinical illness such as hepatitis B, systemic lupus erythematosus, malignancy, or pharmacological side effects (secondary membranous nephropathy or SMN).[9,10]

The clinical presentation is similar in primary and secondary MN. Diagnosis is based on history, Clinical Examination of the patient, Immunofluorescence & Electron microscopy analysis of renal biopsy and circulating antibodies. In most cases, MN is an autoimmune disease caused by autoantibodies directed against phospholipase A2 receptor (PLA2R), thrombospondin type-1 domain-containing (THSD7A) & other newer antigens. PLA2R1 (70–80% of IMN) and THSD7A (3–5% of IMN), the two primary podocyte antigens found in adult IMN may be detected by both direct immunofluorescence labelling of renal tissue and detection of their autoantibodies in blood for diagnosis and prognosis.[9]

The identification of the pathologic events underlying a secondary MN is of paramount importance, since the eradication of the etiologic factors may be followed by remission or definitive cure of MN. The pathogenetic mechanism of Indigenous medicine/drug-induced MN is probably due to an immune response to the drug or the by-product that act as planted antigen on the subepithelial position of the GBM.[11] In a study done by Kumar MN et al similar patients who have been diagnosed as Secondary Membranous Nephropathy due to indigenous medicine intake, 11 cases had high level of mercury in serum and urine and concluded that most patients eventually recover without chelation after stopping the drugs.[12]

## Conclusion

Primary and secondary membranous nephropathy share similar clinical and pathological characteristics. Since traditional medicines are widely used in our nation, it is critical that Clinicians get a relevant history of indigenous medicine use in cases of membranous nephropathy, particularly when PLA2R antibody is negative. Once the definitive diagnosis is reached, patient should abstain from using indigenous medicines and managed conservatively and using Immuno-suppression in selected cases.



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