Utility of Determining Autoantibodies to M-type Phospholipase A2 Receptor in Diagnosing Primary Membranous Nephropathy: An Ideal Setting

Sir,

Primary membranous nephropathy (PMN) is an autoimmune disease caused by autoantibodies to M-type phospholipase A_2 receptor ($aPLA_2R$) and thrombospondin type-1 domain containing 7A.[1] The autoantibodies are helpful in differentiating primary and secondary membranous nephropathy and also have a very good correlation to clinical activity.[1] Can $aPLA_2R$ alone be used to diagnose PMN in clinical situations, where there is contraindication for biopsy, is a question that needs to be answered. The present report highlights one such situation, where $aPLA_2R$ was used to diagnose PMN.

A 30-year-old gentleman with swelling of both lower limbs and facial puffiness was referred to our unit for further management. The patient had no history suggestive of connective tissue disease or past chronic viral disease. On examination, the patient had blood pressure of 120/76 mmHg, and the systemic examination was not contributory. Urine examination revealed 4+ albuminuria (7.50 g/day), with no erythrocytes or leukocytes. Serum creatinine and albumin were 1.30 mg/dl and 1.30 g/dl, respectively. Serum tested negative for hepatitis B surface antigen, hepatitis C virus, human immunodeficiency virus, monoclonal proteins, and anti-nuclear factor. With a provisional diagnosis of adult-onset nephrotic syndrome (NS), kidney biopsy was planned on a day care basis. Ultrasonography revealed small left kidney with stone of 8 mm and normal right side kidney. On the day of biopsy, the patient reported with swelling of the left upper limb. Color Doppler revealed venous thrombosis of the left upper limb. The patient was started on unfractionated heparin and warfarin (INR 2.1). To rule out malignancy-related NS, a positron emission tomography was performed and did not reveal any hypermetabolic area. The index case had two relative contraindications for kidney biopsy; deep vein thrombosis

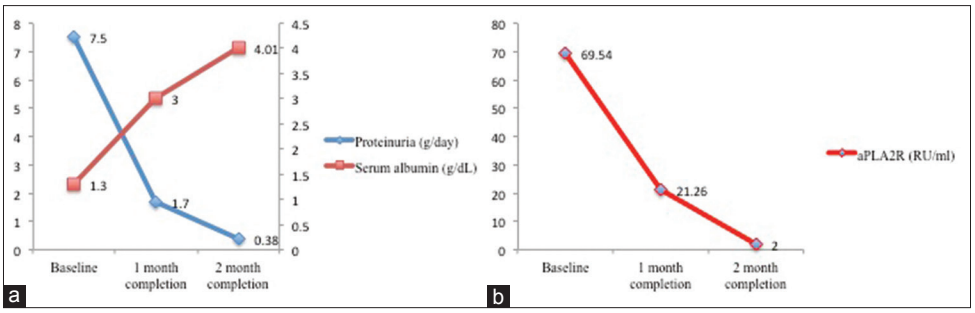

Figure 1: (a) Proteinuria and serum albumin at baseline and after 1 and 2 months of therapy and (b) sequential autoantibodies to M-type phospholipase A_2 receptor titer during the course of therapy

on anticoagulation therapy and contracted left kidney. As knowing that the basic disease would dictate further therapy, serum for $aPLA_2R$ (ELISA, EUROIMMUN, Lubeck, Germany) was performed. ELISA results >20 RU/mL are considered positive. The serum tested positive for $aPLA_2R$ (69.24 RU/mL), and a diagnosis of $aPLA_2R$ related PMN was made. The patient was started on cyclical cyclophosphamide and steroids. After 2 months of starting therapy, the patient had reduction in proteinuria (0.38 g/day) and improvement in serum albumin (4.01 g/dl) [Figure 1a]. Repeat serum $aPLA_2R$ at 1 and 2 months of therapy was 21.23 and <2.00 RU/mL, respectively [Figure 1b].

The present report highlights the diagnostic utility of $aPLA_2R$ in a difficult situation. There has always been a question, "whether $aPLA_2R$ estimation could replace a kidney biopsy in diagnosing PMN?" Well, $aPLA_2R$ alone (without glomerular staining) is of diagnostic value in at least two-thirds of the PMN cases and is a positive step toward simplifying management in patients with NS.[1] However, as with other biomarkers, $aPLA_2R$ reduces our dependence but does not completely substitute a kidney biopsy as the technique not only helps in establishing diagnosis, but also prognosticates. As of date, none of the existing serum or urine biomarker is useful in predicting glomerular and tubulointerstitial (activity and chronicity) minutiae. As words of wisdom clearly state "for the foreseeable future, the practice of clinical nephrology will depend heavily on the kidney biopsy."[2]

The present report highlights an ideal situation for $aPLA_2R$ in diagnosing PMN. The index case had deep venous thrombosis (on anticoagulation) along with contracted left kidney, making it impossible for kidney biopsy. In spite of being valuable, kidney biopsy being invasive in nature is limited by its morbidity and occasional mortality as a follow-up tool. $aPLA_2R$ has a very good association with clinical response and would be helpful in predicting remission, relapse, and/or resistance.[3-6] In the present case, the patient had serial decrease in proteinuria [Figure 1a] and $aPLA_2R$ titer [Figure 1b] with immunosuppressive therapy, confirming both serological and clinical remission.

In spite of having a diagnostic utility, the prominent role of $aPLA_2R$ is currently limited to assess disease activity, especially while deciding second-line therapy for a resistant disease. However, if we are unable to perform a renal biopsy, $aPLA_2R$ could be conveniently used to diagnose PMN after ruling out secondary causes such as malignancy and viral disease with appropriate investigations.

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Conflicts of interest

There are no conflicts of interest.

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