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Membranous nephropathy and primary biliary cholangitis: A case report and review of the literature

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Abstract. Aim: Membranous nephropathy (MN) and primary biliary cholangitis (PBC) are autoimmune diseases that coexist in some cases and might share a common pathogenesis. In 75 – 80% of MN patients, PLA_2R1 or THSD7A is the target antigen responsible for disease development, while in the remaining cases, MN pathogenesis is not clear. Our aim was to identify potential antigens playing an overlapping pathogenic role for development of both PBC and MN. Materials and methods: Serum from a patient with PBC-associated MN was analyzed for MN and PBC-specific autoantibodies and kidney biopsy tissue was stained for the respective antigens. A review of the literature for published PBC-associated MN cases was performed. Results: A 39-year-old male patient was diagnosed with PBC-associated MN. Serology tests revealed negativity for PLA_2R1-ab and THSD7A-ab, but positivity for two PBC-specific antibodies: M2-ab and gp210-ab. Kidney biopsy was stained for both PBC-specific antigens, PDC-E2 and gp210, as well as PLA_2R1 and THSD7A, showing no MN-specific positivity. Human glomerular extracts also did not contain PDC-E2 or gp210. A review of all 17 published cases of PBC-associated MN showed that 71% of patients suffered from at least one additional autoimmune disease, and different IgG-subclasses were found in the renal immune deposits of these patients. Conclusion: These results indicate that both PBC-antigens are not the putative antigen(s) leading to MN development in this patient. PBC-antigens might not be directly responsible for MN development. Both diseases seem to present as autoimmune phenomena triggered by interaction between unknown factors.

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Introduction

Membranous nephropathy (MN) is an autoimmune disease of the kidney and the most frequent cause of nephrotic syndrome in Caucasians adults [1]. In 20 – 25% of cases, MN has been attributed to a multitude of underlying conditions like certain malignancies, autoimmune diseases, infections (i.e., hepatitis), and medications [2] and is considered to be of secondary origin. However, in ~ 75 – 80% of cases, MN develops as a primary autoimmune process, and circulating autoantibodies bind to antigens on the podocytes. The identification of two podocyte-specific antigens, the phospholipase A_2 receptor 1 (PLA_2R1) and the thrombospondin type 1 domain containing protein 7A (THSD7A), which account for 70 – 80% and 2 – 3% of MN patients, respectively, allows MN to be classified by its pathogenic antigens as PLA_2R1- or THSD7A-associated MN [3, 4, 5, 6]. Moreover, PLA_2R1-antibody levels are relevant for treatment management and disease prognosis, while THSD7A-antibodies were detected in some malignancy-associated cases of MN, in which simultaneously diagnosed tumors were found to express THSD7A [3, 6, 7, 8]. Meanwhile, a number of new potential target antigens have been identified in patients with MN, including exostosin 1/exostosin 2, neural epidermal growth factor-like 1 protein (NELL-1), and semaphorin 3B [9, 10, 11].

Some of the most common autoimmune diseases associated with MN are systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), Hashimoto thyroiditis, Graves' disease, and Sjogren's syndrome [2, 12, 13,