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De Novo PLA2R Positive Membranous Nephropathy following BNT162b2 mRNA Covid-19 vaccine

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To the editor,

We report a case of de novo anti-phospholipase A2 receptor (PLA2R) positive membranous nephropathy (MN) following the second dose of the BNT162b2 mRNA Covid-19 vaccine.

A 22-year-old Caucasian male, with a past medical history of eczema and epilepsy, presented with progressive lower limb oedema and lethargy in the month following his second dose of BNT162b2 mRNA Covid-19 vaccine. He had no prior SARS-CoV-2 infection. His vital signs were within normal limits and physical examination revealed bilateral pitting oedema to the sacrum. Laboratory investigations revealed a serum albumin of 8 g/L, an elevated total cholesterol of 22.8 mmol/L, preserved kidney function with a serum creatinine of 64 μmol/L. A spot urine albumin-to-creatinine ratio was 700.4 mg/mmol (normal range <2.5), approximating 7g/day of albuminuria (24-hour urine collection not performed). Renal biopsy confirmed membranous nephropathy (Figure 1a) with positive PLA2R antigen on immunoperoxidase staining. Serum anti-PLA2R autoantibody was positive (118 RU/ml) and the remaining autoimmune and viral screens were unremarkable. Despite three months of conservative management with perindopril, frusemide and anticoagulation, his proteinuria and peripheral oedema worsened. At this time, a rituximab regimen was initiated, followed by partial remission at 2 months (Figure 1b). The patient was referred to the COVID allergy vaccination clinic where the recommendation was to receive a booster dose (mRNA-1273 SARS-CoV-2 vaccine. He tolerated this well without evidence of relapse. Whether this was related to his immunosuppression treatment (rituximab) or, potentially, from additional reduced antibody formation due to renal protein wasting is unclear.

Membranous nephropathy (MN) is an immune mediated glomerular disease. In approximately 70% of primary cases, the target podocyte antigen in this condition is the M-Type receptor for secretory phospholipase A2 (1). However, the exact mechanism of anti-podocyte production in MN remains unclear. Serum levels of PLA2R antibodies often correlate strongly with disease activity (2). Our

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observation, in conjunction with case reports of both de novo disease and relapse of PLA2R positive MN following COVID-19 vaccination (3, 4)—as well as following COVID-19 infection (4, 5)—raise the possibility of immune dysregulation leading to the loss of tolerance to PLAR2 antigen after COVID-19 infection or vaccination.

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Figure legend

Figure 1. (a) Strong global granular capillary wall staining for PLA2R antigen (original magnification x 400) and (b) Timeline of clinical features and management following administration of the COVID-19 vaccine and rituximab treatment.

Figure 1a

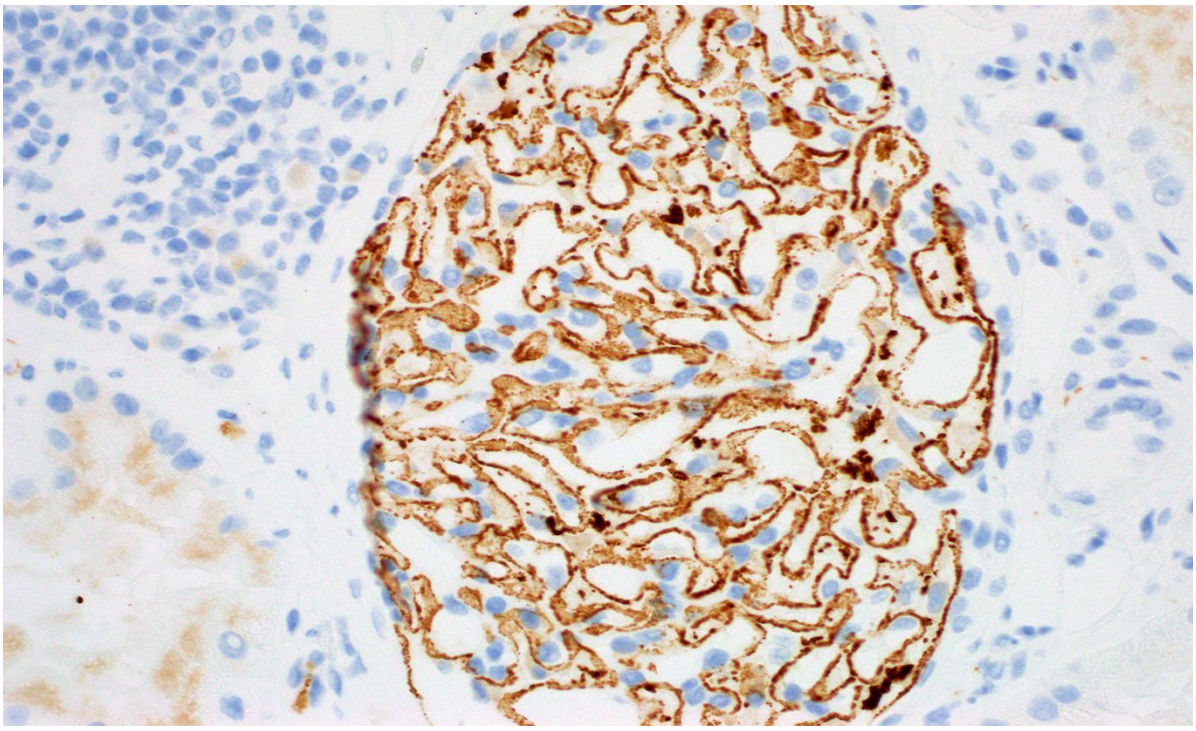

Figure 1b