

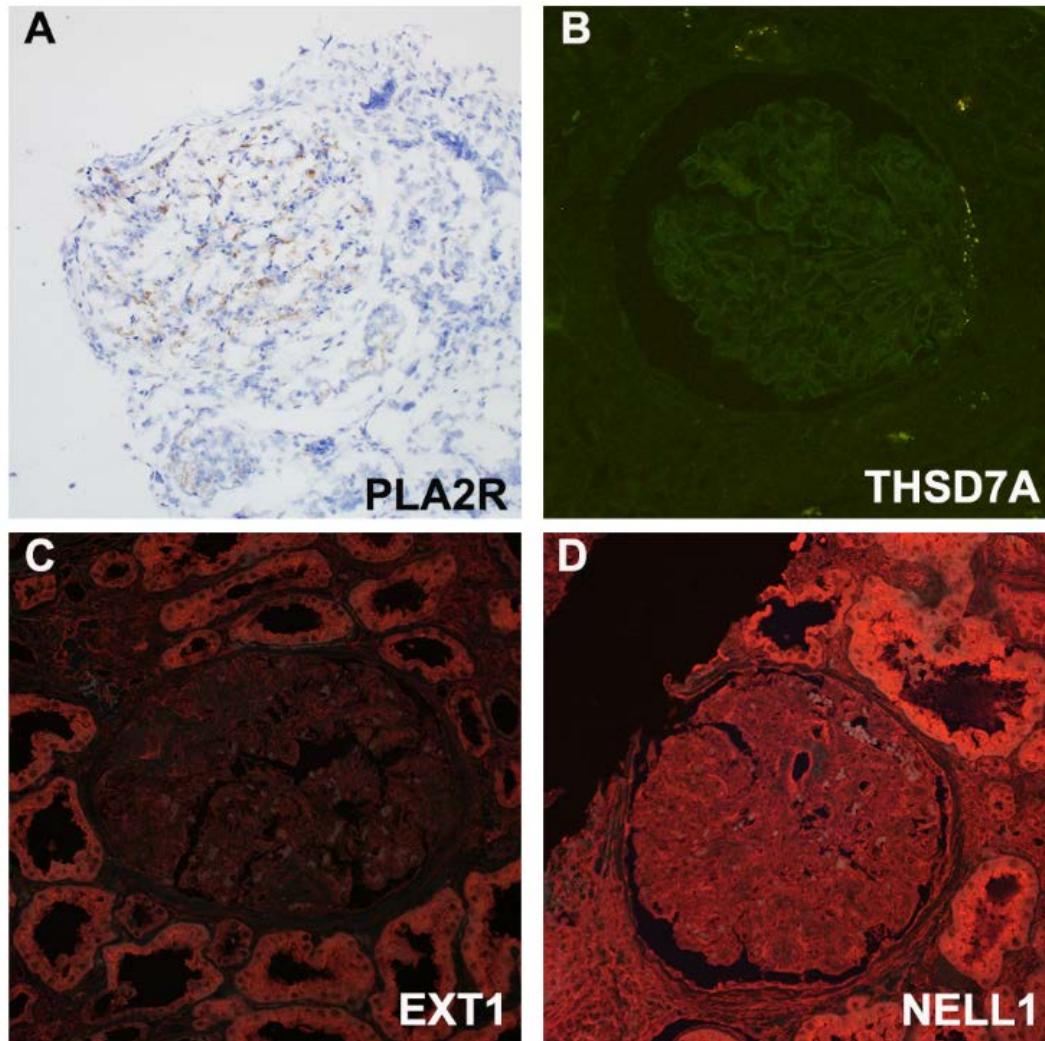
**Supplemental TOC**

**Supplemental Figure 1.** Membranous glomerulopathy in CVID patients is PLA2R (A), THSD7A (B), EXT (C), and NELL1 (D) negative for granular capillary loop staining.

**Supplemental Table 1.** Co-morbid conditions in CVID patients with kidney disease.

**Supplemental Table 2.** Histopathology and follow-up data from patients with common variable immunodeficiency

**Supplemental Figure 1.** Membranous glomerulopathy in CVID patients is PLA2R (A), THSD7A (B), EXT (C), and NELL1 (D) negative for granular capillary loop staining.



**Supplemental Table 1.** Co-morbid conditions in CVID patients with kidney disease.

Clinical characteristics and co-morbid conditions of CVID patients, including developmental, hematologic, cardiovascular, pulmonary, gastrointestinal, endocrine/metabolic, oncologic, and rheumatologic conditions, are shown. Additional values in parentheses ( ) indicate that in addition to this case series, these manifestations have been reported within the literature for CVID patients with renal disease.

Abbreviations: AIHA=autoimmune hemolytic anemia; ITP=idiopathic thrombocytopenic purpura; T-LGL=T-large granular lymphocytosis; CAD = coronary artery disease; CVA = cerebrovascular accident; TIA = transient ischemic attack; COPD = chronic obstructive pulmonary disease; OSA = obstructive sleep apnea; GERD = gastroesophageal reflux disease; IBD = inflammatory bowel disease; PUD = peptic ulcer disease; SLE = systemic lupus erythematosus.

| Category       | Disease manifestation | Membranous nephropathy | Tubulointerstitial nephritis | Other  |
|----------------|-----------------------|------------------------|------------------------------|--------|
| Developmental  | Short stature         | 2                      | 0                            | 0 (+1) |
|                | Developmental delay   | 2 (+1)                 | 0                            | 0      |
|                | Failure to thrive     | 2                      | 0 (+1)                       | 0 (+1) |
| Hematologic    | Anemia                | 2                      | 0                            | 1      |
|                | Thrombocytopenia      | 2 (+1)                 | 0                            | 0      |
|                | Eosinophilia          | 1                      | 0                            | 0      |
|                | AIHA                  | 0                      | 1                            | 0      |
|                | ITP                   | 0                      | 1 (+1)                       | 0 (+1) |
|                | Lymphadenopathy       | 2 (+1)                 | 1 (+1)                       | 0      |
|                | T-LGL lymphocytosis   | 1                      | 1                            | 0      |
|                | Non-Hodgkin lymphoma  | 2                      | 0                            | 0      |
|                | Hemachromatosis       | 0                      | 1                            | 0      |
| Cardiovascular | Hypertension          | 7                      | 0                            | 2      |
|                | Hyperlipidemia        | 1                      | 0                            | 2      |
|                | Atrial fibrillation   | 1                      | 0                            | 0      |

|                       |                               |   |        |        |
|-----------------------|-------------------------------|---|--------|--------|
|                       | CAD                           | 1 | 0      | 0      |
|                       | CVA or TIA                    | 2 | 0      | 1      |
|                       | Bicuspid aortic valve         | 1 | 0      | 0      |
|                       | VSD                           | 1 | 0      | 0      |
| Pulmonary             | COPD                          | 3 | 1      | 1      |
|                       | OSA                           | 2 | 0      | 1      |
|                       | Granulomatous inflammation    | 1 | 1      | 0      |
|                       | Asthma                        | 5 | 0      | 0      |
| Gastrointestinal      | GERD                          | 1 | 0      | 0 (+1) |
|                       | IBD                           | 2 | 0      | 0      |
|                       | Liver disease                 | 2 | 0      | 0      |
|                       | PUD                           | 0 | 0      | 1      |
|                       | Autoimmune enteritis / Celiac | 0 | 1 (+1) | 0      |
|                       | Eosinophilic esophagitis      | 2 | 0      | 0      |
|                       | Ulcerative colitis            | 1 | 0      | 0      |
| Endocrine & metabolic | Obesity                       | 4 | 0      | 0      |
|                       | Hypothyroidism                | 4 | 0 (+1) | 1 (+1) |
|                       | Diabetes                      | 1 | 0      | 1      |
|                       | Hypogonadism                  | 1 | 0      | 0      |
|                       | Gynecomastia                  | 0 | 0      | 1      |
| Oncologic             | Cancer                        | 2 | 2      | 1      |
| Rheumatologic         | Arthritis                     | 0 | 1      | 1      |
|                       | SLE                           | 0 | 1 (+1) | 1      |
|                       | Sjogren's                     | 0 | 1      | 0      |
|                       | Spondylitis                   | 0 | 1      | 0      |
|                       | Meniere's disease             | 0 | 0      | 1      |

**Supplemental Table 2. Histopathology and follow-up data from patients with common variable immunodeficiency**

| Pt | Diagnosis   | Age | Sex | Cr  | Prot     | Immuno-fluorescence   | Inflammation                          | Patient medications  | Treatment for Kidney Disease                     | Outcomes   |
|----|---|-----|-----|-----|----------|---|---------------------------------------|--|--|--|
| 1  | Acute interstitial nephritis, immune complex glomerulopathy                           | 25  | F   | 1.5 | 0.2      | IgG 2+, C3 2+, kappa 2+, lambda 2+, subepithelial + mesangial | Mixed T/B, CD4: CD8 = 70:30           | Azithromycin, Augmentin, IVIG                                      | Splenectomy                                      | Cr reduced to 1.2 mg/dL  |
| 2  | Acute interstitial nephritis, immune complex crescentic GN                            | 44  | F   | 4.4 | None     | IgG 1+, C3 3+, mesangial                                      | >95% T cell CD4: CD8 = 40:60          | Antibiotics for pneumonia (not specified)                          | Prednisone                                       | Cr reduced to 0.9 mg/dL  |
| 3  | Chronic active tubulointerstitial nephritis   | 35  | M   | 3.4 | 2+ on UA | None  | >95% T, CD4:CD8 40:60                 | Hydralazine, Bystolic, Norvasc, IVIG                               | Methylprednisolone, followed by prednisone taper | CKD V, Cr = 6.9 mg/dL, BM bx w/ lymphoma                       |
| 4  | Chronic active tubulointerstitial nephritis   | 24  | F   | 2.3 | 0.5      | IgG trace, kappa trace, lambda trace                          | 100% T, CD4:CD8 70:30                 | Esomeprazole, Mycophenolate mofetil, Prednisone, Ondansetron, IVIG | Prednisone, mycophenolate mofetil                | CKD3, Cr 1.7 mg/dL, GFR = 34 mL/min                            |
| 5  | Ischemic glomerulopathy, Moderate interstitial inflammation                           | 39  | F   | 1.3 | 1.2      | None  | >90% T, CD4:CD8 80:20                 | Infliximab, IVIG   | Infliximab                                       | CKD3, Cr = 2.5 mg/dL, UPC = 1 g/g.                             |
| 6  | Chronic active tubulointerstitial nephritis, mild mesangial immune complex deposition | 44  | M   | 2.5 | None     | IgG 2+, C3 1+, kappa 2+, lambda 2+, mesangial and             | Severe, >95% T cells, CD4:CD8 = 20:80 | Prednisone, Dexilant, Tramadol, IVIG                               | Prednisone                                       | CKD3B, Cr = 2.7 mg/dL, GFR = 26 mL/min, developed Burkitt-like |

|    |  |    |   |     |          | paramesangial   |                                      |  |  | B cell lymphoma   |
|----|--|----|---|-----|----------|---|--------------------------------------|--|--|---|
| 7  | Chronic active tubulointerstitial nephritis        | 24 | F | 2.6 | 0.495    | None  | Severe, 100% T cells, CD4: CD8 90:10 | Prednisone, Mycophenolate mofetil, IVIG  | Prednisone, ID workup ruled out infectious etiology                | Cr 1.7 mg/dL, GFR 34 mL/min                               |
| 8  | Membranous glomerulopathy                          | 42 | F | 1.8 | 4.6      | IgA trace, IgG 2+, kappa 2+, lambda 2+  | None                                 | Lopressor, Norvasc, Cyclobenzaprine, Trazadone, Paxil, Flonase, Hydrochlorothiazide, Xanax, IVIG | IVIG therapy, no immunosuppression.                                | CKD3, Cr 2.1 mg/dL, GFR = 33 mL/min                       |
| 9  | Membranous, glomerulomegaly w/ segmental sclerosis | 20 | M | 1.5 | 0.2      | IgG 2+, kappa 2+, lambda 2+, subepithelial + intramembranous                          | None                                 | Azithromycin, Levothyroxine, IVIG  | No therapy provided.   | Proteinuria remains < 1 g/24 h.                           |
| 10 | Membranous, glomerulomegaly w/ segmental sclerosis | 38 | F | 1.9 | 3+ on UA | IgG2+ C3 trace, kappa 2+, lambda 2+, subepithelial                                    | Moderate, mixed                      | Amlodipine, Lisinopril, Bacrim, Rituximab, Zevalin, IVIG   | Rituximab, Lisinopril  | Persistent proteinuria, history of lymphoma in remission. |
| 11 | Membranous glomerulopathy                          | 10 | M | 0.5 | 0.6      | IgA 1+, IgG 3+, IgM 1+, C3 1+, subepithelial, intramembranous, and mesangial deposits | None                                 | Cyclophosphamide, Escitalopram, Montelukast, Mycophenolate mofetil, Omeprazole                   | IV cyclophosphamide, mycophenolate mofetil for maintenance therapy | Stable renal function.                                    |

|    |   |    |   |     |     |  |      |   |   |   |
|----|---|----|---|-----|-----|--|------|---|---|---|
| 12 | Membranous glomerulopathy                             | 54 | M | 1.0 | 5   | IgA 2+, IgG 3+, C3 3+, kappa 3+, lambda 3+, subepithelial, subendothelial, mesangial                   | None | Lisinopril, Furosemide, Spironolactone, Amlodipine, Levothyroxine, Albuterol, Lexapro, Singulair, Wellbutrin XL, IVIG       | Lisinopril, Losartan                            | Stable renal function, Cr 1.0 mg/dL, proteinuria reduced to 2 g/g, GFR = 81 mL/min. |
| 13 | Membranous glomerulopathy, thrombotic microangiopathy | 68 | M | 8.7 | 1.0 | IgG 2-3+, IgA 2+, IgM 1+, C3 3+, C1q 2+, kappa 3+, lambda 3+, subepithelial, subendothelial, mesangial | None | Metoprolol, Unasyn, Prednisone  | Corticosteroids.                                | Patient died soon after biopsy.   |
| 14 | Membranous glomerulopathy, focal crescents            | 15 | M | 0.3 | 14  | IgG 2+, C3 trace, kappa 2+, lambda 2+, subepithelial and intramembranous                               | Mild | Sirolimus, Budenoside, Mycophenolate mofetil, Rituximab, Amitriptyline, Amlodipine, Gabapentin, Megestrol, Mesalamine, IVIG | Sirolimus, Budesonide, Mycophenolate, Rituximab | Cr 0.4 mg/dL, proteinuria remained (>1000 mg/dL), low albumin (2.2 g/dL)            |
| 15 | Membranous glomerulopathy                             | 70 | F | 0.8 | 1.5 | IgG trace, IgM trace, C3 trace, kappa trace, lambda trace, subepithelial +                             | Mild | Albuterol, Amlodipine, Aspirin, Azelastine, Biotin, Calcium, CoQ-10, Dulera, Duloxetine, Fish oil, Flaxseed Oil, IVIG       | None  | Cr 0.7 mg/dL, 24 h protein 420 mg, GFR 90 mL/min stable renal function              |

|    |   |    |   |     |      |  |   |  |   |
|----|---|----|---|-----|------|--|---|--|---|
|    |   |    |   |     |      |  |   |  |   |
| 16 | Sclerosing glomerulonephritis   | 40 | F | 2.8 | None | intramembranous  |   |  |   |
|    |   |    |   |     |      | Segmental fibrinogen staining within a single glomerulus | Mild, within fibrotic interstitium                    | Unknown, no data available   | Not treated, as no active crescents   |
| 17 | Nodular diabetic glomerulosclerosis                                     | 69 | F | 2.6 | 10   | IgM 1+, mesangial  | Mild, patchy  | Coreg, Verapamil, Isosorbide, Bumex, Amaryl, Glipizide, Linagliptin, Lantus, Aranesp, IVIG   | ESKD (biopsy had 90% interstitial fibrosis)   |
| 18 | Proliferative glomerulonephritis with monoclonal IgG deposits           | 67 | F | 0.8 | 2    | IgG 3+, IgM 2+, C3 3+, kappa 3+, IgG3 restricted         | Mild  | Carvedilol, Aspirin, Cephalexin, Cetirizine, Cyclobenzaprine, Estropipate, Famciclovir, Ferrous sulfate, Fluticasone, Furosemide, Glycopyrrolate, Lansoprazole, Losartan, Mirabegron, Oxybutynin, Phenobarbital, Ranitidine, Sucralfate, Hydralazine | Hematologic workup with no clonal process identified, patient was not treated       |
| 19 | AL amyloidosis, Lambda light chain cast nephropathy, Lambda light chain | 56 | F | 1.4 | 11.8 | 3+ lambda  | Dense, patchy infiltrate at corticomedullary junction | NSAIDS, IVIG   | Chemotherapy and bone marrow transplant<br>Cr 1.5 mg/dL, UPCR 0.1 g/g, in remission |

|    |                                    |    |   |     |      |  |             |  |  |  |
|----|------------------------------------|----|---|-----|------|--|-------------|--|--|--|
|    | proximal tubulopathy               |    |   |     |      |  |             |  |  |  |
| 20 | C3 glomerulopathy                  | 19 | F | 1.9 | 1.4  | C3 2+, subepithelial and intramembranous, paraffin IF negative | Mild, mixed | Mesalamine, Azathioprine, Amlodipine, Budesonide, Dicyclomine, Furosemide, Lisinopril, Olopatadine, Pentasa, Vyvanese, IVIG                          | Lisinopril, ACTHar, Mycophenolate mofetil  | Cr 1.9 mg/dL, UPCR reduced to 0.7 g/g, GFR = 30 mL/min |
| 21 | Acute tubular injury               | 64 | F | 5.5 | None | None   | None        | Loratadine/Pseudo ephedrine, Hydrochlorothiazide, Simvastatin, Lisinopril, Aspirin, Calcium w/ vitamin D, Beta-carotene, acetaminophen, NSAIDs, IVIG | Supportive care, patient developed anuria after laminectomy surgery, which resolved. | Came off dialysis. Cr = 3.0 mg/dL.                     |
| 22 | Thin glomerular basement membranes | 39 | F | 0.9 | 0.1  | 2+ C3, mesangial   | None        | Unknown, no data available   | None   | Stable renal function                                  |