# SUPPLEMENTAL MATERIAL

## Kidney biopsy findings in patients with SARS-CoV-2 infection or after COVID-19 vaccination

Maria Mercedes Noriega MD[#], Faeq Husain-Syed MD[#], Sonia Wulf MLA, Benjamin Csala, Christian F. Krebs MD, Wolfram J. Jabs MD, Peter F. Zipfel PhD, Hermann-Josef Gröne MD, Thorsten Wiech MD, and the CoV-Kidney Investigators

[#]Joint first authors.

CoV-Kidney Investigators: Frank Aedtner MD, Mustafa Bačinović MD, Susanne Bartel-Kuss MD, Alexander Bauer MD, Joachim Beige MD, Horst-Walter Birk MD, Bernhard Böll MD, Philipp Brylka MD, Wolfgang Clasen MD, Süha Dasdelen MD, Maria-Magdalena Eicher MD, Amr Elnaggar MD, Alexander Farid MD, Johannes Francois MD, Jens Gerth MD, Annette Helmke MD, Helen Hepburn MD, Markus Hollenbeck MD, Tobias B. Huber MD, Birgit Jennert MLA, Christoph Jüttner MD, Akel Khaled MD, Kazuhiro Kobayashi MD, Monika Koop MD, Kamil Kuczkowski MD, Martin Loyen MD, Maida Mahmud MD, Cornelia Marczynski MD, Tobias N. Meyer MD, Martin Nitschke MD, Michael A. Reiter MD, Claudio Ronco MD, Norbert Schleucher MD, Diana Schmerler MD, Elisa Alba Schmidt MD, Rüdiger Schmidt MD, Michael Schmitz MD, Werner Seeger MD, Jochen Selbach MD, Lorenz Sellin MD, Fabian Srugies MD, Agnieszka Swiecicka, Sibylle von Vietinghoff MD, Clemens Weinberg MD, Ulrich Wenzel MD, Stephan Christian Werth MD

This supplemental material has been provided by the authors to give readers additional information about their work.

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## SUPPLEMENTAL METHODS

### *Data collection*

Demographic data, medical history, clinical findings, and laboratory data were recorded by the investigators if considered relevant to the observed histopathologic findings of the kidney biopsies. Data were stored in a password-protected dataset. The Hessian Data Protection Act (HDSG, §33) was followed in data collection and publication. Hypertension was defined as based on self-reporting physician diagnosis and/or anti-hypertension medication use. Diabetes mellitus was defined as based on self-reporting physician diagnosis and/or diabetic medication use.

Medications, including potential nephrotoxic agents (e.g., non-steroidal anti-inflammatory drugs, piperacillin-tazobactam, vancomycin) were documented. Laboratory findings collected by the investigators, depending on availability, included platelet count, hemolysis parameters, fragmentocytes, serum creatinine (sCr), urine protein-creatinine ratio, urine albumin-creatinine ratio (ACR), urine α1-microglobulin-creatinine ratio, urine dipstick and sediment analyses, immunological findings (antinuclear antibody, anti-double stranded DNA-antibodies, anti-neutrophil cytoplasmatic antibody, anti-proteinase 3-antibodies, anti-myeloperoxidase-antibodies, anti-glomerular basement membrane-antibodies, anti-M-type phospholipase A2 receptor-antibodies, anti-cardiolipin-antibodies, anti-cyclic citrullinated peptide), complement C3 and C4, mutation of complement regulators, and ADAMTS13. Microbiological and virological findings collected included enterohemorrhagic E. coli-polymerase chain reaction in stool specimens, antistreptolysin-O titer, anti-DNase B titer, hantavirus-specific-antibodies, and SARS-CoV-2 anti-spike IgG antibodies. Treatment and outcome measures (antibiotic therapy, corticosteroid therapy, respiratory support, kidney replacement therapy [KRT], sepsis, death) were documented.

### *Participating centers*

The German participating centers that have sent native kidney biopsies (total amount of biopsies, $n = 27$) from patients vaccinated for COVID-19 were: Caritas-Krankenhaus Bad Mergentheim GmbH, Bad Mergentheim ($n = 2$), University Clinic of the Rheinische Friedrich Wilhelms University Bonn, Bonn ($n = 1$), Knappschaftskrankenhaus Bottrop GmbH, Bottrop ($n = 1$), Städtisches Klinikum Dresden, Dresden ($n = 2$), Heinrich-Heine University Düsseldorf, Düsseldorf ($n = 2$), University Hospital Giessen and Marburg, Giessen ($n = 4$), AMEOS-Klinikum Halberstadt GmbH, Halberstadt ($n = 2$), Asklepios Klinik Barmbek, Hamburg ($n = 1$), Marienkrankenhaus GmbH, Hamburg ($n = 1$), University Hospital Hamburg Eppendorf, Hamburg ($n = 3$), Hospital St. Georg, Leipzig ($n = 1$), University Hospital Schleswig-Holstein, Campus Lübeck, Lübeck ($n = 2$), Klinikum-Passau, Passau ($n = 1$), Klinikum Osnabrück GmbH, Osnabrück ($n = 1$), Agaplesion Diakonieklinikum Rotenburg, Rotenburg an der Wümme ($n = 1$), and Städtisches Klinikum Solingen, Solingen ($n = 2$).

The German participating centers that sent native kidney biopsies from patients with COVID-19 (total amount of biopsies, $n = 15$) were: Vivantes Klinikum im Friedrichshain, Berlin ($n = 4$), Vivantes Humboldt-Klinikum, Berlin ($n = 1$), Klinikum Garmisch-Partenkirchen, Garmisch-Partenkirchen ($n = 1$), University Hospital Hamburg Eppendorf, Hamburg ($n = 4$), Katholisches Karl-Leisner-Klinikum, Kleve ($n = 1$), Herz-Jesu-Hospital Hiltrup GmbH, Münster ($n = 1$), Segeberg Kliniken GmbH, Bad Segeberg ($n = 1$), Evangelisches Krankenhaus Wesel, Wesel ($n = 1$), and Heinrich-Braun-Klinikum, Zwickau ($n = 1$).

### *CoV-Kidney Investigators*

Department of Nephrology and Diabetology, AMEOS-Klinikum Halberstadt GmbH, Gleimstraße 5, 38820 Halberstadt, Germany (Frank Aedtner MD)

Dialysezentrum Rotenburg, Burgstrasse 5, 27356 Rotenburg, Germany (Mustafa Bačinović MD; Johannes Francois MD)

Department of Nephrology, Städtisches Klinikum Solingen, Gotenstraße 1, 42653 Solingen, Germany (Susanne Bartel-Kuss MD)

Department of Internal Medicine, Segeberg Kliniken GmbH, Krankenhausstraße 2, 23705 Bad Segeberg, Germany (Alexander Bauer MD; Alexander Farid MD)

Department of Infectious Diseases/Tropical Medicine, Nephrology and Rheumatology, Hospital St. Georg, Delitzscher Str. 141, 04129 Leipzig, Germany (Diana Schmerler MD; Joachim Beige MD)

Kuratorium for Dialysis and Transplantation (KfH) Renal Unit, Hospital St. Georg, 04129 Leipzig, Germany; Department of Internal Medicine II, Martin-Luther-University Halle/Wittenberg, 06108 Halle/Saale, Germany (Joachim Beige MD)

Department of Internal Medicine II, University Hospital Giessen and Marburg, Justus-Liebig-University Giessen, Klinikstrasse 33, 35392 Giessen, Germany (Horst-Walter Birk MD; Birgit Jennert MLA; Werner Seeger MD)

Department of Medicine I, Klinikum Passau, Innstraße 76, 94032 Passau, Germany (Bernhard Böll MD)

Department of Internal Medicine, Katholisches Karl-Leisner-Klinikum, Albersallee 5-7, 47533 Kleve, Germany (Philipp Brylka MD; Akel Khaled MD)

Herz-Jesu-Hospital Hiltrup GmbH, Westfalenstrasse 109, 48165 Münster, Germany (Martin Loyen MD; Wolfgang Clasen MD)

Department of Nephrology, Vivantes Humboldt-Klinikum, Am Nordgraben 2, 13509 Berlin Reinickendorf, Germany (Agnieszka Swiecicka; Süha Dasdelen MD)

Department of Urology, Klinikum Garmisch-Partenkirchen, Auenstraße 6, 82467 Garmisch-Partenkirchen, Germany (Maria-Magdalena Eicher MD; Michael A. Reiter MD)

Department of Nephrology and Rheumatology, Knappschaftskrankenhaus Bottrop GmbH, Osterfelder Strasse 157, 46242 Bottrop, Germany (Amr Elnaggar MD; Markus Hollenbeck MD)

Department of Internal Medicine II, Division of Nephrology, Heinrich-Braun-Klinikum, Karl-Keil-Strasse 35, 08060 Zwickau, Germany (Jens Gerth MD)

Department of Medicine I, Klinikum Osnabrück GmbH, Am Finkenhügel 1, 49076 Osnabrück, Germany (Annette Helmke MD; Christoph Jüttner MD)

Department of Nephrology, Vivantes Klinikum im Friedrichshain, Landsberger Allee 49, 10249 Berlin-Friedrichshain, Germany (Helen Hepburn MD)

III. Department of Medicine, University Medical Center Hamburg-Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany (Ulrich Wenzel MD; Maida Mahmud MD; Elisa Alba Schmidt MD; Tobias B. Huber MD)

Nephropathology Section, Institute of Pathology, University Medical Center Hamburg-Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany; Gifu University Hospital, 1-1 Yanagido, Gifu City 501-1194, Japan (Kazuhiro Kobayashi MD)

Department of Medicine III, Caritas-Krankenhaus Bad Mergentheim GmbH, Uhlandstraße 7, 97980 Bad Mergentheim, Germany (Monika Koop MD)

Department of Cardiology, Nephrology and Dialysis, Evangelisches Krankenhaus Wesel, Schermbecker Landstraße 88, 46485 Wesel, Germany (Kamil Kuczkowski MD; Rüdiger Schmidt MD)

Department of Medicine I, Städtisches Klinikum Dresden, Friedrichstraße 41, 01067 Dresden, Germany (Cornelia Marczynski MD)

Department of Nephrology, Asklepios Klinik Barmbek, Rübenkamp 220, 22307 Hamburg, Germany (Clemens Weinberg MD; Tobias N. Meyer MD)

Department of Medicine I, Section Nephrology, Dialysis and Transplantation, University Hospital Schleswig-Holstein, Campus Lübeck, Ratzeburger Allee 160, 23562 Lübeck, Germany (Martin Nitschke MD)

University of Padua, Department of Medicine (DIMED), Via Giustiniani, 2–35128 Padua, Italy; International Renal Research Institute of Vicenza, Department of Nephrology, Dialysis and Transplantation, San Bortolo Hospital, Viale Rodolfi, 37–36100 Vicenza, Italy (Claudio Ronco MD)

Department of Oncology and Hematology, Marienkrankenhaus GmbH, Alfredstrasse 9, 22087 Hamburg, Germany (Norbert Schleucher MD)

Department of Nephrology, Städtisches Klinikum Solingen, Gotenstraße 1, 42653 Solingen, Germany (Michael Schmitz MD)

Universities of Giessen and Marburg Lung Center (UGMLC), Member of the German Center for Lung Research (DZL); Max Planck Institute for Heart and Lung Research, Department of Lung Development and Remodelling, Ludwigstrasse 43, 61231 Bad Nauheim, Germany; Institute for Lung Health (ILH), Justus-Liebig-University Giessen, Aulweg 123, 35390 Giessen, Germany (Werner Seeger MD)

Department of Medicine III, Caritas-Krankenhaus Bad Mergentheim GmbH, Uhlandstraße 7, 97980 Bad Mergentheim, Germany (Jochen Selbach MD)

Department of Nephrology, Medical Faculty, Heinrich-Heine University, Moorenstrasse 5, 40225 Düsseldorf, Germany (Fabian Srugies MD, Lorenz Sellin MD)

First Medical Clinic, Nephrology Section, University Clinic of the Rheinische Friedrich Wilhelms University Bonn, Venusberg Campus 1, 53127, Bonn, Germany (Sibylle von Vietinghoff MD)

Department of Medicine I, Section Nephrology, Dialysis and Transplantation, University Hospital Schleswig-Holstein, Campus Lübeck, Ratzeburger Allee 160, 23562 Lübeck, Germany (Stephan Christian Werth MD)

***Procedures***

**Histologic processing of kidney biopsies**

The light microscopy and immunohistochemistry samples were placed in 4% buffered formalin and processed using standard techniques; all biopsies were examined after staining with hematoxylin and eosin, periodic acid–Schiff, and tri-chrome stains. Immunohistochemistry staining for myoglobin was performed in cases with COVID-19. Immunohistochemistry sections were pretreated with protease solutions for antigen retrieval and incubated with antibodies specific for IgG, IgA, IgM, fibrinogen/fibrin, C3, C1q, C4d, and C5b-9 (staining protocols are provided in Supplemental Table 1). Tissue submitted for electron microscopy were buffered (10 min at 80 °C in sodium cacodylate), processed in 1% osmium tetroxide and sucrose (2 h). After washing in cacodylate buffer and 1 h contrasting in uranyl acetate, the specimens were dehydrated in an ascending ethanol series and diethyl ether. The samples were embedded in araldite and polymerized 12 h up to 100 °C. Staining with toluidine blue of the semi-thin sections was performed. Ultra-thin sections were stained with lead citrate. Images were taken using a transmission electron microscope (Zeiss EM109) equipped with a digital camera (TRS 2K-CCD).

**Kidney function measures**

Acute kidney injury (AKI) was defined as an increase in sCr by ≥0.3 mg/dl within 48 h or ≥1.5-times the baseline value within 7 d based on the Kidney Disease: Improving Global Outcomes (KDIGO) AKI guidelines (1). The kidney disease nomenclature was based on the 2020 KDIGO recommendations (2). Kidney recovery was defined as the absence of any stage of AKI based on sCr (3). Complete remission of nephrotic syndrome was defined as a decrease in urine protein-to-creatinine ratio to <200 mg/g and serum albumin to >3.5 g/dl, while partial remission was defined as proteinuria reduction of ≥50% from the presenting value (4). Baseline sCr used was the most recent sCr value from a minimum of 7 d before vaccination or COVID-19 diagnosis. The estimated glomerular filtration rate (eGFR) was determined using the 2009 Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation based on sCr (5). For children under 19 years (case V21), the eGFR was calculated using the creatinine-based "Bedside Schwartz" equation (6). CKD was defined as a known pre-existing kidney disease recorded in the patient's medical record, prior eGFR values <60 ml/min/1.73 $m^2$, or, if available, other pathologic kidney findings (e.g., ACR ≥30 mg/g creatinine, previous pathologic kidney-histopathologic findings) (7). Use of KRT was at the discretion of the attending physician.

**Laboratory methods**

The creatinine level was measured at the local laboratory department. Proteinuria, albuminuria, and α1-microglobulin excretion were normalized to the urine creatinine concentration to account for dilution.

**SUPPLEMENTAL TABLES**

***Supplemental Table 1:*** **Immunohistochemistry staining protocols.**

| **Antibody** | **Firm** | **Pretreatment** | **Dilution** | **Detection system** |
|---|---|---|---|---|
| IgA | DAKO A0262 | Protease | 1:8,000; 30 min | APAAP |
| IgG | Dianova 209- 005-088 (Jackson Immuno Research) | Protease | 1:7,500; 30 min | APAAP |
| IgM | DAKO A0425 | Protease | 1:3,000; 30 min | APAAP |
| C1q | DAKO A0136 (Biomol) | Protease | 1:1,500; 30 min | APAAP |
| C3c | DAKO A0062 | Protease | 1:3,000; 30 min | APAAP |
| Myoglobin | Novus Biologicals, NB120-9536 | Autoclave pH 6.2 | 1:600; overnight | ABC-Vector* |
| PLA2R1 (p) | Sigma HPA012657 | Autoclave pH 6,2 | 1+1,500 + 1+3,000 overnight | Zytomed |

*ABC Vector stain Elite Kit (Vector Laboratories, Burlingame, CA, USA).

APAAP, alkaline phosphatase-anti-alkaline phosphatase; C1q, complement C1q; C3, complement C3; PLA2R1, M-type phospholipase A2 receptor type 1.

***Supplemental Table 2:*** **Questionnaire on patients with COVID-19 vaccination.**

| **Baseline clinical data** |
|---|
| Medical history |
| Comorbidities |
| Baseline serum creatinine (date of the measurement) |
| Baseline proteinuria, albuminuria, and α1-mikroglobulin excretion (date of the measurement) |
| Baseline hematuria / acanthocyturia (if available) (date of the measurement) |
| Contact number of the primary care physician/primary care nephrologist |
| **Post-vaccination data** |
| Vaccine regimen (date of vaccination) |
| Symptoms after vaccination (date of symptoms) |
| Date of admission / biopsy indication |
| Serum creatinine around the time of biopsy / peak serum creatinine (date of the measurement) |
| Proteinuria, albuminuria, and α1-mikroglobulin excretion around the time of biopsy (date of the measurement) |
| Baseline hematuria / acanthocyturia around the time of biopsy (date of the measurement) |
| Serology/laboratory findings (e.g., ANA, ANCA, anti-GBM-ABs, complement C3/C4, cryoglobulin, PLA2R- and THSD7A-ABs, rheumatoid factor, and anti-CCP, hantavirus-specific ABs, blood culture) |
| SARS-CoV-2 anti-nucleocapsid and anti-spike antibodies (date of the measurement) |
| Kidney-related risk factors |
| Kidney replacement therapy / other therapies |
| Kidney- and non-kidney-related outcomes including laboratory data; name/contact number of the primary care nephrologist |

ABs, antibodies; ANA, antinuclear antibody; ANCA, anti-neutrophil cytoplasmatic antibody; anti-CCP, anti-cyclic citrullinated peptide; COVID-19, coronavirus disease 2019; GBM, glomerular basement membrane; anti-PLA2R-AB, anti-M-type phospholipase A2 receptor antibody; SARS-CoV-2, severe acute respiratory syndrome coronavirus type 2; THSD7A-AB, thrombospondin type 1 domain-containing 7A autoantibodies.

***Supplemental Table 3:*** **Questionnaire on patients with SARS-CoV-2 infection.**

| |
|---|
| **Baseline clinical data** |
| Medical history |
| Comorbidities |
| Baseline serum creatinine (date of the measurement) |
| Baseline proteinuria, albuminuria, and α1-mikroglobulin excretion (date of the measurement) |
| Baseline hematuria / acanthocyturia (if available) (date of the measurement) |
| Contact number of the primary care physician/primary care nephrologist |
| **Clinical data during COVID-19** |
| Date of admission / biopsy indication |
| Serum creatinine around the time of biopsy / peak serum creatinine (date of the measurement) |
| Proteinuria, albuminuria, and α1-mikroglobulin excretion around the time of biopsy (date of the measurement) |
| Baseline hematuria / acanthocyturia around the time of biopsy (date of the measurement) |
| Serology/laboratory findings (e.g., ANA, ANCA, anti-GBM-ABs, complement C3/C4, cryoglobulin, PLA2R- and THSD7A-ABs, rheumatoid factor, and anti-CCP, hantavirus-specific ABs, blood culture) |
| Risk factors for AKI (e.g., ventilation, nephrotoxin exposure, rhabdomyolysis, hemorrhage, sepsis, organ failure) |
| COVID-19 therapy (e.g., corticosteroids, chloroquine, monoclonal antibodies, convalescent plasma) |
| Kidney replacement therapy / other therapies |
| Kidney- and non-kidney-related outcomes including laboratory data; name/contact number of the primary care nephrologist |

ABs, antibodies; AKI, acute kidney injury; ANA, antinuclear antibody; ANCA, anti-neutrophil cytoplasmatic antibody; anti-CCP, anti-cyclic citrullinated peptide; COVID-19, coronavirus disease 2019; GBM, glomerular basement membrane; GN, glomerulonephritis; anti-PLA2R-AB, anti-M-type phospholipase A2 receptor antibody; SARS-CoV-2, severe acute respiratory syndrome coronavirus type 2; THSD7A-AB, thrombospondin type 1 domain-containing 7A autoantibodies.

***Supplemental Table 4*: Demographic data, clinical information and laboratory findings of patients who underwent kidney biopsy after receiving COVID-19 vaccination.**

| Pt | Baseline data | | | | | | | | Post-vaccination data | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Age, y** | **Sex** | **HTN/DM present** | **CKD status** | **sCr (mg/dl)/eGFR (ml/min/1.73 m$^2$)[a,b], (time of assessment before vaccination)** | **PCR/ACR (mg/g creatinine)** | **Urine dipstick/sediment analyses** | **Other findings** | **Vaccine regimen** | **Day of symptoms post-vaccination; Day of admission** | **Kidney presentation/biopsy indication** | **Peak sCr (mg/dl)[a] before biopsy (Day of biopsy post-vaccination)** | **PCR/ACR /α1MGCR before kidney biopsy (mg/g creatinine)** | **Urine dipstick/urine sediment analyses** | **Other findings** | **Outcome** |
| **Necrotizing GN** | | | | | | | | | | | | | | | | |
| V1 | 82 | F | None | No history of CKD | 0.69/81 (32 mo) | Negative protein dipstick | Erythrocyte count 10/µl; leukocyte count 15/µl | Interstitial lung disease, status after ANA-positive autoimmune hepatitis | Homologous BNT162b2/ BNT162b2 (Pfizer/BioNTech) | Day 2 after the second dose (progressive deterioration of general health, weakness, generalized pain, proximal muscle weakness, particularly in the thighs, pain when chewing); admission on Day 35 after the second dose | Suspected MPO-ANCA positive vasculitis (kidney involvement with increased proteinuria, myositis, vasculitis of the left temporal artery) | 0.55 (Day 44) | 376/98/– | Erythrocyte count 100–200/µl; leukocyte count 50/µl | pANCA 1:1000, elevated anti-MPO-ABs (>134 U/ml), negative for anti-PR3-ABs; ANA 1:320, elevated rheumatoid factor (111 IU/ml); anti-CCP in normal range; wall thickening of left temporal artery (MRI); myositis of thighs (MRI and EMG) | Monthly i.v. cyclophosphamide, prednisolone (1 mg/kg/d for 7 d, followed by a taper); clinical improvement at discharge (sCr 0.57 mg/dl) |
| V2 | 81 | F | HTN | Unknown | N/A | N/A | N/A | – | Homologous BNT162b2/ BNT162b2 | ~Day 35 after the second dose (deterioratio | AKI, suspected rapidly progressive | 4.5 (Day 48) | 2,385/ 2,208/96 | Erythrocyte dipstick 2+, | Positive ANCA >1:160, anti- | Monthly i.v. cyclophosphamide, |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | (Pfizer/BioNTech) | n of general health, progressive edema); admission on Day 42 due to progression of symptoms | glomerulonephritis due to MPO-ANCA positive vasculitis | | | acanthocyturia 20%; negative leukocyte dipstick, leukocyte count 8/µl | MPO-ABs >200 U/ml | prednisolone (1 mg/kg/d for 7 d followed by a taper); initiation of maintenance hemodialysis on Day 40 post-biopsy due to progressive kidney disease (sCr 5.60 mg/dl) and associated complications (e.g., volume overload, pneumonia) |
| V3 | 60 | M | HTN | Unknown | 1.21/65 (31 mo) | Negative protein dipstick | Negative erythrocyte and leukocyte dipstick | – | Homologous BNT162b2/ BNT162b2 (Pfizer/BioNTech) | Day 1 after the second dose (deterioration of general health, fatigue); admission on Day 34 after the second dose | AKI, suspected MPO-ANCA positive rapidly progressive glomerulonephritis | 12.23 (Day 40) | –/561/– | Erythrocyte dipstick 1+; erythrocyte count 536/µl; negative leukocyte dipstick, leukocyte | Positive pANCA 1:10 and positive anti-MPO-ABs; ANA 1:100, negative results for anti-PR3-ABs, anti-dsDNA-ABs, and anti-GBM-ABs; C3/C4 in the normal range; | No established immunosuppressive therapy considering the advanced histological kidney disease; ultimately referral to maintenance hemodialysis |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | count 82/μl | negative hantavirus-specific ABs | |
| V4 | 81 | M | HTN/DM II | No history of CKD | 1.14/60 (11 mo) | N/A | N/A | History of urothelial carcinoma | Heterologous ChAdOx1 nCoV-19/ mRNA-1273 (Oxford/AstraZeneca/Moderna Biotech) | Day 3 after the second dose (deterioration of general health, joint and muscle pain, dyspnea); admission Day 12 after the second dose due to progression of symptoms | Suspected PR3-ANCA positive vasculitis (pulmonary-renal syndrome with pulmonary infiltrates and AKI likely due to rapidly progressive glomerulonephritis) | 1.52 (Day 23) | 750/–/– | Erythrocyte dipstick 3+, erythrocyte count 1/μl, positive acanthocyturia; negative leukocyte dipstick, leukocyte count 0/μl | Elevated anti-PR3-ABs (>200 U/ml), negative for anti-MPO-ABs; ANA 1:80, negative for anti-dsDNA-ABs, rheumatoid factor, and anti-CCP | Monthly i.v. cyclophosphamide, prednisolone (1 mg/kg/d for 7 d followed by a taper); partial kidney recovery at discharge (sCr 1.39 mg/dl) |
| V5 | 60 | M | HTN | No history of CKD | 0.91/90 (1 mo) | 81.6/11.2 | N/A | Surgically-treated abscess on the forefoot 1 mo before vaccination | Single dose of Ad26.COV2.S (Janssen-Cilag, Johnson & Johnson) | Day 5 (nonproductive cough, fever with chills, joint pain, edema, maculopapular rash with palpable purpura); admission Day 15 post-vaccination due to progressive edema, and elevated C-reactive protein and sCr | Suspected rapidly progressive glomerulonephritis (KRT-dependent AKI, NRP, leukocytoclastic vasculitis) | 15.04 (Day 19) | 7,712/ 2,834/334 | Erythrocyte dipstick 3+, erythrocyte count 9 849/μl, negative acanthocyturia, leukocyte dipstick 1+ | Negative for ANA, anti-dsDNA-ABs, ANCA, anti-GBM-ABs, and hantavirus-specific-ABs; C3/C4, ASO titer, and anti-DNase B titers in the normal range; no evidence of abscess/osteomyelitis of the forefoot | Monthly i.v. cyclophosphamide, prednisolone 250 mg for 3 d, followed by 1 mg/kg/d for 7 d, followed by a taper; remain on maintenance hemodialysis 3 mo post-biopsy |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | | | (MRI); anti-spike IgG ABs 667.6 AU/ml (Day 21 post-vaccination) | |
| V6 | 71 | M | HTN | No history of CKD | 1.00/75 (4 mo) | Negative protein dipstick | Negative erythrocyte und leukocyte dipstick | Non-small cell lung cancer, first diagnosed 2 mo before vaccination, ongoing chemoradiotherapy (carboplatin/paclitaxel); status after AKI post-chemo with partial recovery (sCr max. 2.47 mg/dl, sCr at discharge 1.71 mg/dl) | Homologous BNT162b2/ BNT162b2 (Pfizer/BioNTech) | Day 6 after second dose (progressive fatigue, acid reflux); admission Day 10 after second dose due to progression of symptoms and elevated sCr | AKI, nephritic urinary sediment | 4.30 (Day 12) | –/398/– | Erythrocyte dipstick 3+; positive acanthocyturia | ANA 1:640, negative for anti-dsDNA-ABs, anti-PR3- and anti-MPO-ABs | Monthly i.v. cyclophosphamide, prednisolone (1 mg/kg/d for 7 d followed by a taper); partial kidney recovery 1 mo post-biopsy (sCr 2.70 mg/dl) |
| V7 | 68 | M | HTN | Stable PR3-AB-positive CKD (ANCA-associated GN, biopsy-proven in 2014) | 1.25/59 (4 mo) | N/A | Erythrocyte dipstick 2+, erythrocyte count 84/µl | Diagnosis of large vessel vasculitis in 2006, stable after cyclophosphamide and methotrexate treatment; no | Homologous BNT162b2/ BNT162b2 (Pfizer/BioNTech) | Day 1–3 after the second dose (deterioration of general health, arthralgia); ~Day 10 after the second dose (swelling of forefoot; treated with | Suspected rapidly progressive glomerulonephritisdue to rising PR3-ABs, nephritic urinary sediment | 1.41 (Day 104) | 3,150/583/ 82 | Erythrocyte dipstick 2+; acanthocyturia 30% | Elevated cANCA (1:80) and anti-PR3-ABs (103 U/ml); negative for anti-MPO-ABs, ANA, anti-dsDNA-ABs, and anti-GBM-AB; | Monthly i.v. cyclophosphamide, prednisolone (1 mg/kg/d for 7 d followed by a taper); progressive kidney disease 1 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | maintenance immunosuppression | | colchicine and prednisolone); Day 100 after the second dose, admission due to persistently elevated C-reactive protein | | | | | cultures: negative; aortic valve vegetation likely due to vasculitis | mo post-biopsy (sCr 3.02 mg/dl, PCR 2 380 mg/g creatinine, ACR 565 mg/g creatinine, α1MGCR 95 mg/g creatinine) |
| V8 | 82 | F | HTN/DM II | Stable CKD | 1.68/28 (5 mo) | –/3 | Erythrocyte count 250/µl | UTI and erysipelas 2 d before vaccination; treated with antibiotics | Single dose of BNT162b2 (Pfizer/BioNTech) | Day 3 (deterioration of general health, anuria, dyspnea, edema); admission Day 4 post-vaccination due to progression of symptoms | KRT-dependent AKI on CKD | 6.6 (Day 4) | 3,700/652/– | Erythrocyte dipstick 3+, erythrocyte count 7/µl, acanthocyturia 1%; negative leukocyte dipstick | Negative for cryoglobulin, ANA, anti-dsDNA-ABs, ANCA, and anti-GBM-ABs; reduced C3 level (21 mg/dl); C4 in the normal range; negative hantavirus-specific ABs; no sign of persistent UTI or erysipelas, negative blood cultures | Prednisolone 0.5 mg/kg/d for 14 d followed by a taper; short-term KRT-dependent at Day 4–30 post-vaccination; partial kidney recovery at discharge (sCr 3.1 mg/dl) |
| **Podocytopathies** | | | | | | | | | | | | | | | | |
| V9 | 48 | F | HTN | Stable CKD (IgA nephropathy, biopsy- | 2.25/25 (16 mo) | 213/152 | Erythrocyte count 10/µl | No immunosuppression (status after mycophen | Homologous BNT162b2/ BNT162b2 (Pfizer/BioNTech) | ~Day 14 after the second dose (transient gross hematuria, | NS, AKI on CKD | 4.26 (Day 93) | 4,056/ 3,154/– | Erythrocyte count 392/µl; negative | ANA 1:80 (SSA-rho positive); Increased anti-MPO-ABs (134 | ACEi and prednisolone 100 mg for 2 d, followed by 1 |

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| | | | | proven in 1991) | | | | olate mofetil therapy); rising anti-MPO-ABs (9.1 IU/ml in 2013; 17 IU/ml in 2017); positive ANA testing (1:1 280 in 2013; 1:320 in 2016), longstanding positive SSA-rho without manifestations | | higher than usual proteinuria, edema); admission Day 92 after the second dose due to progressive edema and hypertension | | | | leukocyte dipstick; negative bacterial count | IU/ml), negative for anti-PR3-ABs | mg/kg/d for 14 d followed by a taper; blood pressure control; ultimately referral to maintenance peritoneal dialysis |
| V10 | 26 | F | None | No history of CKD | 0.75/113 (8 mo) | N/A | N/A | – | Homologous BNT162b2/ BNT162b2 (Pfizer/BioNTech) | Day 0–2 after the second dose (transient edema), ~Day 7 after the second dose (recurrence of edema); admission on Day 37 after the second dose due to progression of symptoms | NS | 0.63 (Day 38) | 4,747/ 3,221/8 | Erythrocyte dipstick 1+, erythrocyte count 23/µl; positive acanthocyturia; negative leukocyte dipstick, leukocyte count 3/µl | Negative for ANA, anti-dsDNA-ABs, ANCA, and anti-GBM-ABs; C3/C4 in the normal range | ACEi and prednisolone 250 mg for 2 d, followed by 1 mg/kg/d for 21 d, followed by a taper; complete remission by Day 7 (sCr 0.92 mg/dl, PCR 10 mg/g creatinine) and Day 22 post-biopsy (sCr 1.01 |

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| | | | | | | | | | | | | | | | | mg/dl, PCR 15 mg/g creatinine) |
| V11 | 25 | M | None | No history of CKD | 0.97/112 (18 mo) | Negative protein dipstick | Negative erythrocyte and leukocyte dipstick | – | Single dose of Ad26.COV2.S (Janssen-Cilag, Johnson & Johnson) | ~Day 41 (fatigue, abdominal/flank pain, progressive edema, increased waist circumference); diagnosis of NS on Day 62; admission on Day 106 post-vaccination based on diagnostic biopsy | NS | 0.87 (Day 106) | 8,550/ 7,950/22 | Negative erythrocyte dipstick, negative acanthocyturia; negative leukocyte dipstick | Negative for ANA, anti-dsDNA-ABs, ANCA, anti-GBM-ABs, PLA2R-ABs, and THSD7A-ABs | ACEi, salt restriction, prednisolone (0.5 mg/kg body weight) and tacrolimus therapy; partial remission 1 mo post-biopsy (ACR 1 020 mg/g creatinine) |
| V12 | 54 | M | None | No history of CKD | 1.24 (3 mo) | N/A | N/A | – | Homologous BNT162b2/ BNT162b2 (Pfizer/BioNTech) | Day 2 after the second dose (fever); Day 14 after the second dose (progressive peripheral edema, diagnosis of deep vein thrombosis); admission Day 96 after the second dose due to severe NS (serum protein 36.1 g/l) | NS | 1.12 (Day 121) | 7,230/ 5,500/123 | Negative erythrocyte dipstick, erythrocyte count 16/µl; leukocyte count 93/µl | Negative for ANA, anti-dsDNA-ABs, ANCA, and anti-GBM-ABs | ACEi and prednisolone 1 mg/kg/d; complete remission 1 mo post-biopsy (sCr 0.84 mg/dl, PCR <100 mg/g creatinine) |

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| V13 | 38 | M | None | No history of CKD | 1.00/96 (35 mo) | N/A | N/A | – | Homologous BNT162b2/ BNT162b2 (Pfizer/BioN Tech) | Day 0–3 after the second dose (headache, fever, deterioration of general health, foamy urine, lid edema, progressive peripheral edema; total intake of 1,600 mg ibuprofen); admission Day 21 after the second dose due to progressive edema | NS | 1.00 (Day 24) | 8,105/ 4,839/40 | Erythrocyte dipstick 1+; negative acanthocyturia; negative leukocyte dipstick | Negative results for ANA, anti-dsDNA-ABs, ANCA, and anti-PLA2R-ABs | ACEi and prednisolone 1 mg/kg/d; partial remission 1 mo post-biopsy (sCr 0.90 mg/dl, ACR 1 341 mg/g creatinine) |
| V14 | 61 | F | None | Unknown | N/A | N/A | N/A | – | Homologous BNT162b2/ BNT162b2 (Pfizer/BioN Tech) | ~Day 24 after the second dose (progressive edema, foamy urine, hypertension; no symptoms after the first dose); admission Day 45 after the second dose due to hypertensive crisis | NS | 0.80 (Day 45) | 7,863/ 6,985/31 | Erythrocyte dipstick 1+, negative acanthocyturia; negative leukocyte dipstick | Negative for ANA, anti-dsDNA-ABs, and ANCA; elevated C3 (158 mg/dl), C4 in the normal range; negative hantavirus-specific ABs | ACEi, salt restriction, statin therapy; partial remission 1 mo post-biopsy without immunosuppressive therapy (sCr 1.17 mg/dl, PCR 600 mg/g creatinine) |
| **Other GN types** | | | | | | | | | | | | | | | | |
| V15 | 35 | M | None | History of CKD of | 1.3/71 (2 mo) | 321/– | Erythrocyte dipstick 3+, | Transient gross hematuria first time | Heterologous ChAdOx1 nCoV-19/ mRNA-1273 | Day 0–1 after the first dose (gross hematuria); | Decreased eGFR and elevated proteinuria | 1.3 (Day 71) | 163/91/5 | Erythrocyte dipstick 3+, | Negative for ANA, anti-dsDNA-ABs, | ACEi and SGLT2-i therapy |

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| | | | | unknown etiology | | | erythrocyte count 200/µl | observed during *Campylobacter jejuni* diarrhea 2 mo before the first dose, which led to the first encounter with a nephrologist and a diagnosis of kidney disease | (Oxford/AstraZeneca/Moderna Biotech) | no symptoms after the second dose; elective admission Day 71 after the second dose for diagnostic biopsy | of unknown etiology, suspected IgA nephropathy | | | erythrocyte count 128/µl, acanthocyturia 12%; negative leukocyte dipstick, leukocyte count 10/µl | ANCA, and anti-GBM-ABs; C3/C4 in the normal range | |
| V16 | 20 | F | None | No history of CKD | N/A | N/A | N/A | Initiation of isotretinoin therapy 9 mo before vaccination | Homologous BNT162b2/ BNT162b2 (Pfizer/BioNTech) | ~Day 10 after the first dose (mild periorbital edema); Day 1 after the second dose (severe periorbital edema for two weeks, followed by progressive peripheral edema); total intake of 5,400 mg ibuprofen due to menstrual abdominal pain; admission Day 18 after the second dose due to progressive | NS | 0.5 (Day 20) | 13,474/ 9,431/– | Erythrocyte dipstick 1+ | Negative for ANA, anti-dsDNA-ABs, ANCA, and THSD7A-ABs; positive for PLA2R-ABs; C3 and C4 in the normal range | ACEi and diuretic therapy; discontinuation of isotretinoin |

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| | | | | | | | | | | edema and hypertensive crisis | | | | | | |
| V17 | 29 | M | None | No history of CKD | 0.8/121 (8 mo) | N/A | N/A | Status after pulmonary arterial embolism 8 mo before vaccination (no peripheral edema at any point before vaccination, serum albumin in the normal range) | Homologous BNT162b2/ BNT162b2 (Pfizer/BioNTech) | Day 3 after the first dose (mild edema); ~Day 2 after the second dose (progressive edema, fatigue, deterioration of general health); admission Day 8 after the second dose | NS | 0.70 (Day 9) | –/6,242/– | Erythrocyte dipstick 1+; negative leukocyte dipstick | Negative for ANA; elevated anti-PLA2R-ABs (700 U/ml) | ACEi therapy; deterioration of kidney disease 1 mo post-biopsy (sCr 1.05 mg/dl, PCR 11,459 mg/g creatinine, ACR 7 014 mg/g creatinine) |
| V18 | 23 | F | None | No history of CKD | 0.89/92 (56 mo) | N/A | N/A | – | Single dose of Ad26.COV2.S (Janssen-Cilag, Johnson & Johnson) | ~Day 3 (fatigue, progressive edema, lymph node swelling; treatment with cefpodoxime); admission Day 70 post-vaccination due to NS | NS | 0.58 (Day 70) | 4,200/ 2,894/– | Erythrocyte dipstick 3+; positive acanthocyturia | Negative for ANA, anti-dsDNA-ABs, and ANCA; C3/C4 in the normal range; serum anti-PLA2R-ABs was not tested | No established therapy except ACEi and diuretics; stable disease at Day 22 post-biopsy (sCr 0.61 mg/dl, PCR 3 900 mg/g creatinine) |
| V19 | 66 | M | HTN/DM II | No history of CKD | 0.85/91 (5 mo) | N/A | N/A | – | Single dose of ChAdOx1 nCoV-19 (Oxford/AstraZeneca) | Day 2 (deterioration of general health, fatigue, myalgia, arthralgia, fever, weight | AKI, elevated proteinuria | 1.51 (Day 136) | 1,234/763/ 20 | Erythrocyte dipstick 2+, erythrocyte count 23/µl, | Negative for ANA, anti-dsDNA-ABs, ANCA, anti-GBM-ABs, and anti-PLA2R- | Prednisolone 0.5 mg/kg/d for 30 d followed by a taper; partial remission |

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| | | | | | | | | | | loss); Day 30 post-vaccination treatment with low-dose prednisolone due to suspected multisystem inflammatory syndrome; admission Day 135 post-vaccination due to symptom progression and persistently elevated C-reactive protein; patient refused to receive the second vaccination | | | | negative acanthocyturia; negative leukocyte dipstick, leukocyte count 50/μl | ABs; negative hantavirus-specific ABs; rheumatoid factor, anti-CCPs, and C3/C4 in the normal range; anti-spike IgG ABs 9.1 AU/ml (Day 25 post-vaccination) | at discharge (1.10 mg/dl, PCR 230 mg/g creatinine) |
| V20 | 68 | M | HTN | No history of CKD | 0.77/98 (22 mo) | N/A | N/A | – | Single dose of BNT162b2 (Pfizer/BioNTech) | ~Day 3 (deterioration of general health; herpes zoster infection; erysipelas); admission Day 45 post-vaccination due to dyspnea and oliguria | AKI | 2.73 (Day 48) | 1,010/–/– | Erythrocyte dipstick 3+, erythrocyte count 239/μl positive acanthocyturia; leukocyte dipstick 1+ | Negative for cryoglobulin, ANA, anti-dsDNA-ABs, ANCA, and anti-GBM-ABs; *Staphylococcus aureus* bacteremia, positive ASO titer | N/A |

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| **Acute tubular injury** | | | | | | | | | | | | | | | | |
| V21 | 20 | M | None | No history of CKD | 0.62/117 (18 mo) | N/A | N/A | – | Single dose of ChAdOx1 nCoV-19 (Oxford/AstraZeneca) | Day 0–2 (abdominal/flank pain, loss of appetite; total intake of 800 mg ibuprofen); admission Day 6 post-vaccination | AKI | 4.20 (Day 8) | –/322/– | Erythrocyte dipstick 2+; negative leukocyte dipstick; negative bacterial count | Negative for ANA, anti-dsDNA-ABs, and ANCA; ASO titer in the normal range | No established therapy; partial kidney recovery 1 mo post-biopsy (sCr 1.1 mg/dl, ACR 8 mg/g creatinine) |
| V22 | 62 | F | HTN/DM II | Stable CKD (nephrosclerosis/diabetic biopsy-proven kidney disease in 2016) | 3.30/14 (4 mo) | 811/– | Negative dipstick | Obesity, heart failure with mid-range ejection fraction | Single dose of BNT162b2 (Pfizer/BioNTech) | ~Day 14 (fatigue, edema); on Day 5 the patient had another intraocular anti-VEGF injection for diabetic macular edema; no NSAID use, no change in maintenance therapy; admission Day 21 post-vaccination due to progression of symptoms | AKI on CKD | 5.80 (Day 28) | 1,200/–/– | Negative erythrocyte and leukocyte dipstick | Negative for ANA, anti-dsDNA-ABs, and ANCA; C3/C4 in the normal range | No established therapy; partial kidney recovery 1 mo post-biopsy (sCr 4.60 mg/dl); planning of arteriovenous fistula surgery |
| V23 | 20 | M | None | No history of CKD | N/A | N/A | N/A | – | Homologous BNT162b2/ BNT162b2 (Pfizer/BioNTech) | Day 1–2 after the second dose (fatigue, progressive flank pain; no | AKI | 3.30 (Day 5) | –/88/– | Negative erythrocyte and leukocy | Negative for ANA, anti-dsDNA-ABs, ANCA, and anti-GBM-ABs; C3/C4, | No established therapy; complete kidney recovery by Day 16 |

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| | | | | | | | | | | symptoms after the first dose); no NSAID use; admission Day 2 after the second dose | | | | te dipstick | rheumatoid factor, and ASO titer in the normal range; negative for hantavirus-specific ABs | post-biopsy (sCr 1.0 mg/dl) |
| V24 | 43 | F | None | No history of CKD | 0.79/92 (4 mo) | Negative protein dipstick | Negative erythrocyte and leukocyte dipstick | – | Homologous BNT162b2/ BNT162b2 (Pfizer/BioNTech) | ~Day 7 after the second dose (deterioration of general health, edema; after the first dose only local injection-site pain); no NSAID use; admission Day 49 after the second dose | KRT-dependent AKI | 15.60 (Day 50) | N/A | N/A | N/A | Short-term KRT for four sessions; partial kidney recovery by Day 15 post-biopsy (sCr 1.7 mg/dl) |
| **Interstitial nephritis** | | | | | | | | | | | | | | | | |
| V25 | 20 | M | HTN | No history of CKD | 0.84/126 (15 mo) | N/A | N/A | – | Single dose of BNT162b2 (Pfizer/BioNTech) | Day 20 (flank pain, fever; treatment with cephalosporin derivate over 3 d; no NSAID use); admission Day 20 post-vaccination due to progression of symptoms | AKI | 4.01 (Day 22) | –/145/– | Negative erythrocyte dipstick, erythrocyte count 1/µl; negative leukocyte dipstick; negative | Negative for hantavirus-specific ABs; C3/C4 in the normal range; ANA, anti-dsDNA-ABs, ANCA, and anti-GBM-ABs were not tested | No established therapy; partial kidney recovery 1 mo post-biopsy (sCr 1.61 mg/dl) |

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| | | | | | | | | | | | | | | bacterial count | | |
| V26 | 54 | F | None | No history of CKD | 0.87/78 (38 mo) | N/A | N/A | – | Homologous BNT162b2/ BNT162b2 (Pfizer/BioNTech) | ~Day 2 after the second dose (nonproductive cough, nausea, fever with chills, acid reflux; no NSAID use, nitrite-negative UTI was treated with penicillin, cephalosporine, and fluoroquinolone derivates; admission Day 40 after the second dose due to progression of symptoms and elevated C-reactive protein/sCr | AKI | 2.57 (Day 43) | 508/ 108/102 | Negative erythrocyte dipstick, erythrocyte count 7/µl; leukocyte dipstick 2+, leukocyte count 154/µl | Negative for ANA, anti-dsDNA-ABs, ANCA, and anti-GBM-ABs; C3/C4 in the normal range; hantavirus-specific ABs not tested; negative for UTI | Prednisolone 1 mg/kg/d for 21 d followed by a taper; partial kidney recovery 1 mo post-biopsy (sCr 1.27 mg/dl) |
| V27 | 81 | F | HTN | No history of CKD | 0.69/83 (22 mo) | N/A | N/A | – | Homologous BNT162b2/ BNT162b2 (Pfizer/BioNTech) | ~Day 50 after the second dose (deterioration of general health, fatigue, loss of appetite, nausea; no NSAIDs use, no change of maintenance medication); admission | AKI | 6.70 (Day 97) | 920/80/378 | Erythrocyte dipstick 2+, erythrocyte count 11/µl, negative acanthocyturia; leukocyte | Negative for ANA, anti-dsDNA-ABs, ANCA, anti-GBM-ABs, and anti-CCP; C3/C4 in the normal range; negative hantavirus-specific | Prednisolone 1 mg/kg/d; partial kidney recovery at discharge (sCr 3.8 mg/dl, PCR 1 102 mg/g creatinine) and at one-month |

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| | | | | | | | | | | Day 78 after the second dose due to elevated sCr and volume overload | | | | dipstick 1+, leukocyte count 12/µl | ABs; elevated rheumatoid factor IgA (31.26 U/ml); negative QuantiFERON-TB Gold test | follow-up (sCr 2.30 mg/dl, PCR 972 mg/g creatinine) |

[a]To convert the sCr values to µmol/l, multiply by 88.4.
[b]The eGFR was calculated using the 2009 CKD Epidemiology Collaboration equation (5), except case V21 in whom it was calculated using the creatinine-based "Bedside Schwartz" equation (6).

ABs, antibodies; ACEi, angiotensin-converting enzyme inhibitor; ACR, urine albumin-to-creatinine ratio; AKI, acute kidney injury; α1MGCR, urine α1-microglobulin-to-creatinine ratio; ANA, antinuclear antibody; ANCA, anti-neutrophil cytoplasmatic antibody; anti-CCP, anti-cyclic citrullinated peptide; anti-dsDNA, anti-double stranded DNA; ASO, anti-streptolysin-O; AU, arbitrary unit; cANCA, cytoplasmatic anti-neutrophil cytoplasmatic antibody; CKD, chronic kidney disease; DM, diabetes mellitus; DM II, type II diabetes mellitus; eGFR, estimated glomerular filtration rate; F, female; EMG, electromyogram; GBM, glomerular basement membrane; GN, glomerulonephritis; HTN, hypertension; IgA, immunoglobulin A; i.v., intravenous; KRT, kidney replacement therapy; M, male; MPO, myeloperoxidase; MRI, magnetic resonance imaging; N/A, not available; mRNA, messenger ribonucleic acid; NRP, nephrotic-range proteinuria; NS, nephrotic syndrome; NSAID, non-steroidal anti-inflammatory drug; PCR, urine protein-to-creatinine ratio; anti-PLA2R-AB, anti-M-type phospholipase A2 receptor antibody; pANCA, perinuclear anti-neutrophil cytoplasmatic antibody; PR3, proteinase 3; SARS-CoV-2, severe acute respiratory syndrome coronavirus type 2; sCr, serum creatinine; SGLT2-i, sodium-dependent glucose co-transporter 2-inhibitor; THSD7A-AB, thrombospondin type 1 domain-containing 7A autoantibodies; UTI, urinary tract infection; VEGF, vascular endothelial growth factor.

***Supplemental Table 5:*** **Demographic data, clinical information, and laboratory findings of patients with SARS-CoV-2 infection who underwent kidney biopsy.**

| Pt | Baseline clinical data | | | | | | | | Clinical data during COVID-19 | | | | | | | | |
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| | **Age, y** | **Sex** | **HTN/DM present** | **CKD status** | **Baseline sCr (mg/dl)/ eGFR (ml/min/ 1.73 m$^2$)[a,b]** | **PCR/ ACR (mg/g creatinine)** | **Urine dipstick/sediment analyses** | **Other findings** | **Kidney presentation/biopsy indication** | **Peak sCr prior to kidney biopsy (mg/dl)[a]** | **PCR/ACR /α1MGCR before kidney biopsy (mg/g creatinine)** | **Urine dipstick/sediment analyses** | **Other findings** | **Risk factors for AKI (other than COVID-19)** | **Need for KRT/other therapies** | **COVID-19 therapy** | **Outcome** |
| | 0 | 0 | 0 | 4 | 4 | 12 | 13 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| **Necrotizing GN** | | | | | | | | | | | | | | | | | |
| C1 | 75 | F | HTN/DM II | Unknown | N/A | N/A | N/A | Rheumatoid arthritis treated with low-dose maintenance prednisolone | Suspected rapidly progressive glomerulonephritisdue to MPO-ANCA positive vasculitis, pulmonary-renal syndrome with AKI and hemoptysis | 4.1 | 3,640/ 2,730/200 | Erythrocyte dipstick 3+, erythrocyte count 24/µl | Positive pANCA, elevated anti-MPO-ABs (>100 U/ml), negative for anti-PR3-ABs; ANA 1:320, negative ENA pool, anti-dsDNA-ABs 40.6 U/ml; complement C3/C4 in the normal range; pulmonary consolidations likely related to hemorrhage or bacterial | Progressive pulmonary consolidations and respiratory failure | KRT | Corticosteroids (as part of vasculitis therapy) | i.v. rituximab, prednisolone (1 mg/kg/d for 7 d); short-term KRT for 1 d; therapy discontinued according to patients' wish; ultimately, the patient died |

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| | | | | | | | | | | | | infiltrates (CT scan) | | | | |
| C2 | 81 | F | HTN/DM II | History of CKD | 3.98/10 (5 mo) | 129/75 | Erythrocyte dipstick 1+, erythrocyte count 50/µl, negative acanthocyturia | Heart failure with preserved ejection fraction | AKI on CKD, suspected rapidly progressive glomerulonephritisdue to MPO-ANCA positive vasculitis | 5.92 | 1,915/1,160/– | Erythrocyte count 21–35/µl; negative acanthocyturia; leukocyte count 6–10/µl | pANCA 1:1000, elevated anti-MPO-ABs (>200 U/ml), negative for anti-PR3-ABs and anti-dsDNA-ABs; ANA 1:320, complement C3/C4 in the normal range | Acute decompensated heart failure | None | None | No established immunosuppressive therapy considering the reduced general condition and advanced histological kidney disease; partial kidney recovery at discharge (sCr 3.60 mg/dl) |
| C3 | 81 | M | None | No history of CKD | 1.1/63 (23 mo) | N/A | N/A | Heart failure with mid-range ejection fraction, chronic obstructive pulmonary disease | Suspected PR3-ANCA positive vasculitis (KRT-dependent AKI likely due to rapidly progressive glomerulonephritis, vasculitis-associated gastric antral ulcer) | 4.15 | (Protein dipstick 3+) | Erythrocyte dipstick 2+ | Elevated anti-PR3-ABs (177 U/ml), negative for anti-MPO- and anti-GBM-ABs; complement C3/C4 in the normal range; ANA and hantavirus-specific-ABs not tested; histologic evidence | Pneumogenic sepsis, vasopressor use | KRT | Dexamethasone | Monthly i.v. cyclophosphamide for 6 mo, prednisolone (1 mg/kg/d for 7 d followed by a taper); short-term KRT with partial kidney recovery (6 mo post-biopsy sCr 1.95 mg/dl, PCR and ACR 668 |

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| **Thrombotic microangiopathy** | | | | | | | | | | | | | | | | | |
| C4 | 24 | F | None | No history of CKD | 0.8/103 (one week) | N/A | N/A | Pregnancy with need for emergency cesarean section due to fetal distress; no sign for HELLP | Postpartum KRT-dependent AKI, suspected DIC/TMA | 3.40 | 1,600/–/– | Erythrocyte dipstick 3+; leucocyte count 500/µl | Negative for ANA, anti-dsDNA-ABs, ANCA, and anti-GBM-ABs; platelet count and complement C3/C4 in the normal range; normal ADAMTS 13 activity; no mutation of the complement regulators | Peripartum hemorrhage with massive blood transfusion and clotting factor replacement; mechanical ventilation | KRT | None | Short-term KRT with partial kidney recovery at discharge (sCr 1.5 mg/dl) |
| C5 | 42 | F | None | No history of CKD | 0.8/91 (two weeks) | N/A | N/A | Pregnancy with need for cesarean section due to fetal distress; pre-partum | Postpartum KRT-dependent AKI, suspected TMA | 6.09 | N/A | N/A | Negative for ANA, anti-dsDNA-ABs, ANCA, and anti-GBM-ABs; thrombocytopenia and hemolytic | Postpartum sepsis with multiple organ failure including cardiomyopathy, suspected HELLP syndrome and DIC, rhabdomyo | KRT | None | Short-term KRT with partial kidney recovery at discharge (sCr 1.2 mg/dl) |

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| | | | | | | | | mild HTN without treatment and mild thrombocytopenia | | | | | anemia; ADAMTS 13 not tested | lysis, mechanical ventilation, vancomycin therapy | | | |
| C6 | 40 | M | None | Unknown | N/A | N/A | N/A | Treatment of naïve multiple sclerosis | AKI with NS, suspected TMA | 8.13 | 14,720/ 8,040/344 | Dipstick 3+; erythrocyte count 171/μl | Negative for EHEC-PCR in stool specimen, HIT, ANA, anti-dsDNA-ABs, ANCA, anti-GBM-ABs, anti-PLA2R-, and anti-cardiolipin-ABs; thrombocytopenia and hemolytic anemia with positive fragmentocytes; normal ADAMTS 13 activity; complement C3/C4 in the normal range; no mutation of the | None | KRT, plasmapheresis, eculizumab | Dexamethasone | Ultimately referral to maintenance hemodialysis |

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| | | | | | | | | | | | | complement regulators | | | | |
| C7[c] | 52 | F | HTN | Stable CKD | 1.5/40 (1 mo) | N/A | N/A | – | KRT-dependent AKI on CKD, suspected TMA | 3.80 | –/2,000/– | Erythrocyte dipstick 2+; leucocyte dipstick 2+ | ANA 1:100 with homogenous nuclear pattern (AC-8); negative for ANCA; normal ADAMTS 13 activity; heterozygous variant c.2792G>A p.(Cys931Tyr) (chr1:g.196709758G>A) in complement factor H | None | KRT, eculizumab | None | Short-term KRT for total 2 mo; ongoing outpatient treatment with i.v. eculizumab; normal kidney function at 9 mo post-biopsy (sCr 1.06 mg/dl) |
| **Podocytopathies** | | | | | | | | | | | | | | | | |
| C8 | 62 | M | HTN/DM II | History of CKD | 1.6/52 (20 mo) | –/123 | N/A | Suspected secondary hypertension | AKI on CKD | 5.10 | –/1,753/– | Erythrocyte dipstick 2+ | ANA, anti-dsDNA-ABs, ANCA, and anti-GBM-ABs not tested; C3/C4 in the normal range | Patient of African origin | None | Dexamethasone | No established therapy except ACEi; partial remission 1 mo post-biopsy (sCr 2.6 mg/dl, ACR 1 735 mg/g creatinine) |
| C9 | 35 | F | None | No history of CKD | 0.60/120 (11 mo) | N/A | N/A | State after HELLP syndro | NS | 0.56 | 7,000/–/– | Erythrocyte dipstick 2+; | Negative for ANA, anti-dsDNA- | None | None | Corticosteroids (as part of | Prednisolone (1 mg/kg/d), ACEi and |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | me twice; obesity | | | | leukocyte dipstick 1+ | ABs, ANCA, and anti-PLA2R-ABs | | | MCD therapy) | statin treatment; partial remission 1 mo post-biopsy (sCr 0.7 mg/dl, ACR 1 200 mg/g creatinine) |
| **Acute tubular injury** | | | | | | | | | | | | | | | | | |
| C10 | 36 | F | HTN | Stable CKD (primary FSGS, biopsy-proven in 1991) | 2.21/28 (6 mo) | 250/60 | Erythrocyte dipstick 1+ | Polyarthritis and pulmonary sarcoidosis treated with azathioprine and low-dose maintenance prednisolone | KRT-dependent AKI on CKD, NS | 13.83 | 27,900/ 14,100/– | Erythrocyte dipstick 1+; erythrocyte count 11/µl | Negative for ANA, anti-dsDNA-ABs, ANCA, and anti-PLA2R-AB; complement C3 in the normal range, elevated complement C4 (900 mg/l) | Non-invasive ventilation | KRT | Dexamethasone | Recurrent pulmonary embolism likely due to NS; ultimately reference to maintenance hemodialysis |
| C11 | 50 | F | HTN | Unknown | N/A | N/A | N/A | – | AKI | 5.99 | 3,551/ 2,050/– | Erythrocyte dipstick 1+ | Negative for ANCA and anti-GBM-ABs; ANA 1:160 with fine speckled pattern (AC-4) | None | None | None | Ultimately reference to maintenance peritoneal dialysis |
| C12 | 22 | M | None | No history of CKD | 0.70/134 (27 mo) | N/A | N/A | – | KRT-dependent AKI, NRP | 15.00 | 18,039/ 12,010/– | Erythrocyte dipstick 3+ | Negative for ANA, anti-dsDNA-ABs, | Piperacillin/tazobactam therapy | KRT | None | Short-term KRT for 17 d with partial kidney |

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| | | | | | | | | | | | | ANCA, and anti-GBM-ABs; positive circulating immune complexes; rhabdomyolysis | | | | recovery at discharge (sCr 1.17 mg/dl; ACR <5 mg/g creatinine) |
| C13 | 51 | M | HTN | No history of CKD | 0.90/99 (16 d) | N/A | N/A | – | AKI, suspected TMA | 6.13 | 1,650/ 1,040/150 | Erythrocyte dipstick 3+; erythrocyte count 236/µl | Negative for EHEC-PCR in stool specimen, ANA, anti-dsDNA-ABs, ANCA, anti-GBM-ABs, and anti-PLA2R-ABs; normal ADAMTS 13 activity; rheumatoid factor, anti-CCP, and complement C3/C4 in the normal range | Frequent NSAID use 3 d before admission; piperacillin/tazobactam therapy | None | None | Partial kidney recovery at discharge (sCr 1.84 mg/dl) |
| C14 | 72 | M | HTN | No history of CKD | 0.94/83 (27 mo) | N/A | N/A | Status: after stroke and left atrial appendage occlusi | KRT-dependent AKI | 11.50 | 2,700/700/ 140 | Erythrocyte dipstick 3+ | Negative for ANA, anti-dsDNA-ABs, ANCA, anti-GBM-ABs, and | Non-invasive ventilation, critical illness | KRT | Dexamethasone | Short-term KRT-dependent on Day 1–4 post-admission, partial kidney |

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| | | | | | | | | on, sleep apnea | | | | | anti-PLA2R-ABs; complement C3/C4 in the normal range | | | | recovery at discharge (sCr 3.09 mg/dl); partial kidney recovery 4 mo post-biopsy (sCr 1.22 mg/dl, PCR 76 mg/g, ACR 13 mg/g creatinine) |
| **Interstitial nephritis** | | | | | | | | | | | | | | | | | |
| C15 | 32 | M | None | Unknown | N/A | N/A | N/A | – | AKI on suspected CKD | 7.69 | 460/199/141 | Negative erythrocyte dipstick, erythrocyte count 7/µl; negative leukocyte dipstick, leukocyte count 8/µl | Negative for ANA, anti-dsDNA-AB, ANCA, and anti-GBM-ABs; complement C3/C4 in the normal range; negative QuantiFERON-TB Gold test; no radiological findings suggestive of sarcoidosis | None (particularly no NSAID use) | None | None | Prednisolone therapy with 1 mg/kg/d for four weeks, followed by a taper; partial kidney recovery at discharge (sCr 5.61 mg/dl) |

[a]To convert the values for sCr to µmol/l, multiply by 88.4.
[b]The eGFR was calculated using the 2009 CKD Epidemiology Collaboration equation (5).

[c]The information provided on Patient C7 has been partially published (8).

ABs, antibodies; ACEi, angiotensin-converting-enzyme inhibitor; ACR, urine albumin-to-creatinine ratio; ADAMTS13, a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13; AKI, acute kidney injury; α1MGCR, urine α1-microglobulin-to-creatinine ratio; ANA, antinuclear antibody; ANCA, anti-neutrophil cytoplasmatic antibody; anti-dsDNA, anti-autologous double-stranded DNA; CKD, chronic kidney disease; COVID-19, coronavirus disease 2019; CT, computer tomography; DIC, disseminated intravascular coagulopathy; DM, diabetes mellitus; DM II, type II diabetes mellitus; EHEC-PCR, enterohemorrhagic E. coli-polymerase chain reaction; eGFR, estimated glomerular filtration rate; ENA, extractable nuclear antigen; F, female; FSGS, focal segmental glomerulosclerosis; GBM, glomerular basement membrane; GN, glomerulonephritis; HELLP, hemolysis, elevated liver enzymes and low platelets; HIT, heparin-induced thrombocytopenia; HTN, hypertension; IgA, IgA; i.v., intravenous; KRT, kidney replacement therapy; M, male; MCD, minimal change disease; NSAID, non-steroidal anti-inflammatory drug; MPO, myeloperoxidase; N/A, not available; NRP, nephrotic-range proteinuria; NS, nephrotic syndrome; pANCA, perinuclear anti-neutrophil cytoplasmatic antibody; PCR, urine protein-to-creatinine ratio; anti-PLA2R-AB, anti-M-type phospholipase A2 receptor antibody; PR3, proteinase 3; sCr, serum creatinine; TMA, thrombotic microangiopathy.

***Supplemental Table 6*: Summary of missing data for patients with COVID-19 vaccination.**

| **Variables** | **Missing data, n (%)** |
|---|---|
| **Baseline data** | |
| Age | 0 (0) |
| Sex | 0 (0) |
| HTN/DM present | 0 (0) |
| CKD status | 3 (11) |
| Baseline serum creatinine/eGFR | 4 (15) |
| PCR/ACR | 17 (63) |
| Urine dipstick/sediment analyses | 17 (63) |
| Other findings | 0 (0) |
| **Post-vaccination data** | |
| Vaccine regimen | 0 (0) |
| Any symptoms post-vaccination (including Day of symptoms); Day of admission | 0 (0) |
| Kidney presentation/biopsy indication (date of biopsy) | 0 (0) |
| Peak serum creatinine (date of the measurement) | 0 (0) |
| PCR/ACR/α1MGCR excretion | 1 (4) |
| Urine dipstick/urine sediment analyses | 1 (4) |
| Other findings | 1 (4) |
| Outcome | 1 (4) |

ACR, urine albumin-to-creatinine ratio; α1MGCR, urine α1-microglobulin-to-creatinine ratio; CKD, chronic kidney disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HTN, hypertension; PCR, urine protein-to-creatinine ratio.

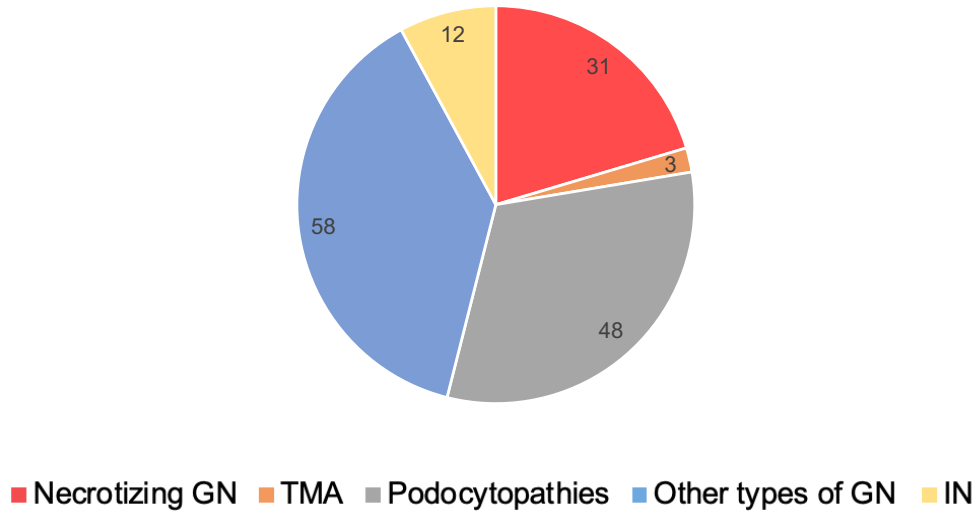
***Supplemental Table 7:*** **Summary of missing data for patients with SARS-CoV-2 infection.**

| **Variables** | **Missing data, n (%)** |
|---|---|
| **Baseline clinical data** | |
| Age | 0 (0) |
| Sex | 0 (0) |
| HTN/DM present | 0 (0) |
| CKD status | 4 (27) |
| Baseline serum creatinine/eGFR | 4 (27) |
| PCR/ACR | 12 (80) |
| Urine dipstick/sediment analyses | 13 (87) |
| Other findings | 0 (0) |
| **Clinical data during COVID-19** | |
| Kidney presentation/biopsy indication (date of biopsy) | 0 (0) |
| Peak serum creatinine (date of the measurement) | 0 (0) |
| PCR/ACR/α1MGCR excretion | 1 (7) |
| Urine dipstick/sediment analyses | 1 (7) |
| Other findings | 0 (0) |
| Risk factors for AKI (other than COVID-19) | 0 (0) |
| Need for KRT/other therapies | 0 (0) |
| COVID-19 therapy | 0 (0) |
| Outcome | 0 (0) |

ACR, urine albumin-to-creatinine ratio; AKI, acute kidney injury; α1MGCR, urine α1-microglobulin-to-creatinine ratio; CKD, chronic kidney disease; COVID-19, coronavirus disease 2019; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HTN, hypertension; KRT, kidney replacement therapy; PCR, urine protein-to-creatinine ratio; sCr, serum creatinine.

**SUPPLEMENTAL FIGURES**

***Supplemental Figure 1:*** **Biopsy-based kidney disease frequencies reported up to August 2022 in adult patients with a temporal association to SARS-CoV-2 vaccination.***

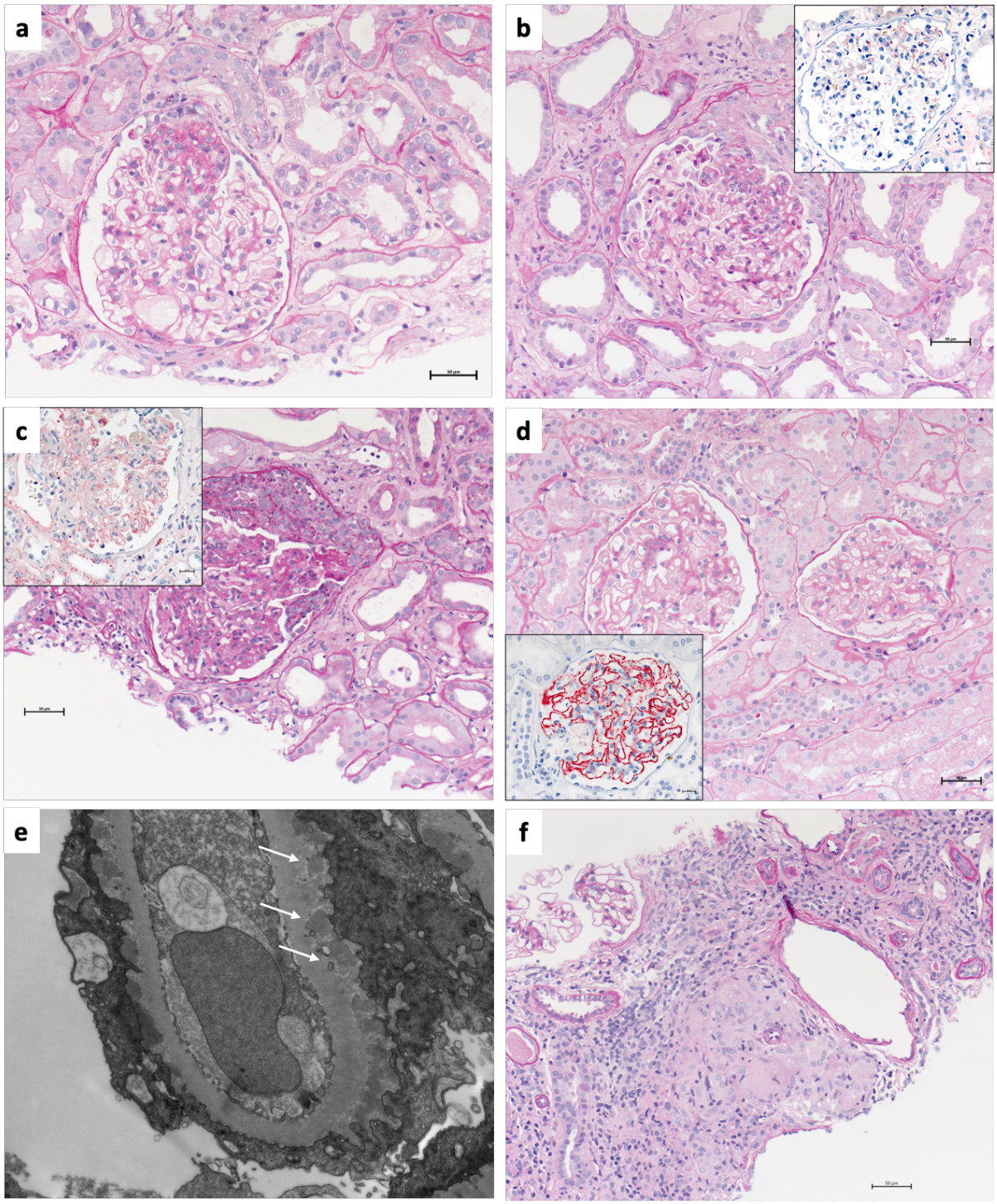



Reported manifestations in native kidney biopsies include necrotizing GN (ANCA-associated GN [*n* = 24; one case also included under 'other GNs'] (9-20), anti-glomerular basement membrane GN [*n* = 3] (10, 21-23), Hepatitis B-associated polyarthritis nodosa [*n* = 1] (16), crescentic IgA nephropathy [*n* = 2] (24, 25), crescentic fibrillary glomerulonephritis [*n* = 1] (26)); TMA [*n* = 3; one case also included under minimal change nephropathy] (27-29), podocytopathies (minimal change nephropathy [n = 39; one case also included under TMA] (9, 10, 23, 27-44), non-collapsing focal segmental glomerulosclerosis [*n* = 5] (10, 23, 38, 44, 45), collapsing glomerulopathy [*n* = 4] (9, 46)), other GNs (IgA nephropathy [*n* = 37] (9-11, 20, 21, 23, 28, 47-53), membranous nephropathy [*n* = 15] (9, 23, 42, 54-57), lupus nephritis [*n* = 5] (9, 23, 58-60), membranoproliferative GN [*n* = 1] (23)), and IN (IN [*n* = 10] (23, 28, 61-63), granulomatous nephritis [*n* = 1] (64), IgG4-related IN [*n* = 1] (65)).

*Includes only cases with new diagnosis of kidney disease (i.e., kidney biopsy after vaccination).

ANCA, anti-neutrophil cytoplasmatic antibody; ATI, acute tubular injury; COVID-19, coronavirus disease 2019; GN, glomerulonephritis; IgA, immunoglobulin A; IN, interstitial nephritis; SARS-CoV-2, severe acute respiratory syndrome coronavirus type 2; TMA, thrombotic microangiopathy.

***Supplemental Figure 2*: Kidney histopathological findings seen in patients after COVID-19 vaccination (panels a–e) or with SARS-CoV-2 infection (panel f).**



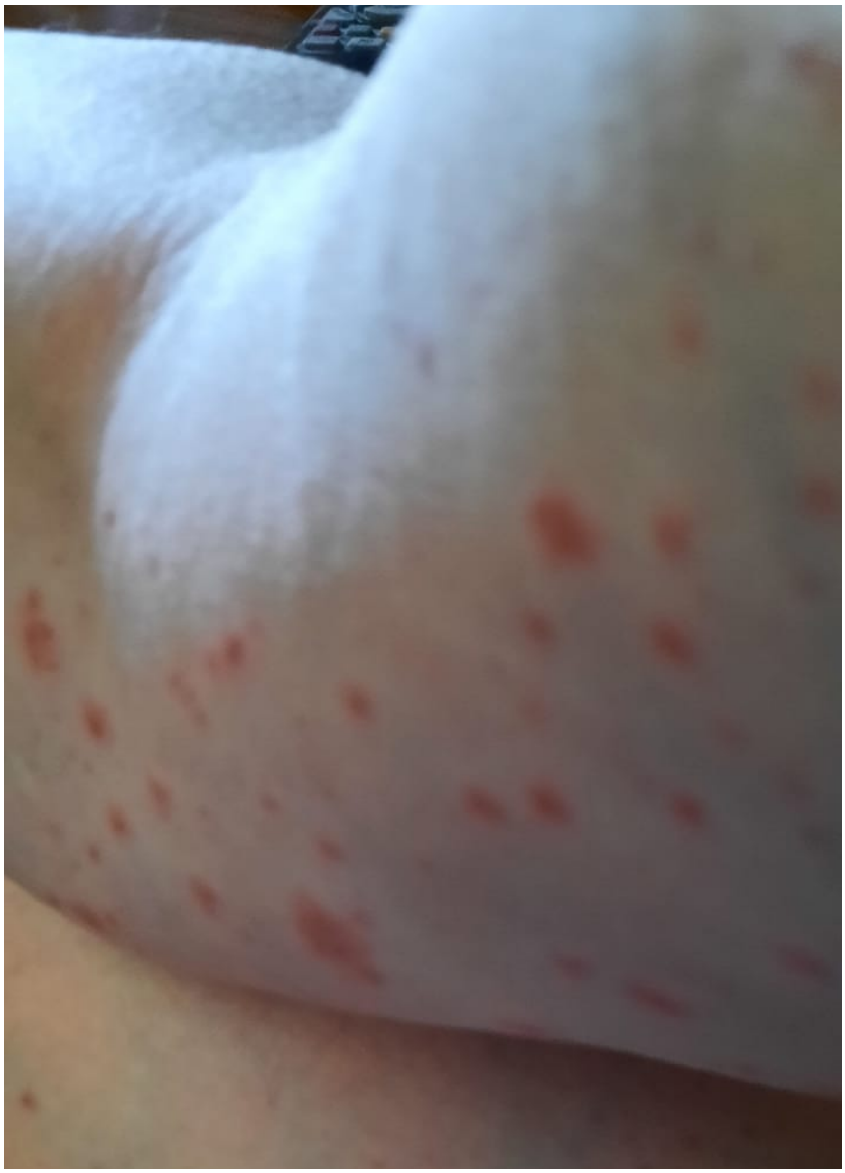

(a) Light microscopy image showing focal segmental glomerulosclerosis in case V13. PAS staining. Magnification, × 200. (b) Light microscopy image showing case V8 with post-/parainfectious GN with cellular crescent (inset shows immunohistochemistry staining for C3). PAS. Magnification, × 200. (c) Light microscopy image showing a lesion of immunocomplex-mediated mesangioproliferative GN with a fibrocellular crescent in case V8 (inset shows immunohistochemistry staining for IgG). PAS. Magnification, × 200. (d) Light microscopy image showing case V18 with membranous nephropathy (inset shows immunohistochemistry staining for IgG4). PAS. Magnification, × 200. (e) Electron micrograph showing subepithelial electron-dense deposits (white arrows) in case V16 with PLA2R1-associated membranous nephropathy. Magnification, × 8,000. (f) Light microscopy

image showing interstitial nephritis with granulomatous components, advanced interstitial fibrosis, and tubular atrophy in case C15. PAS. Magnification, × 100.

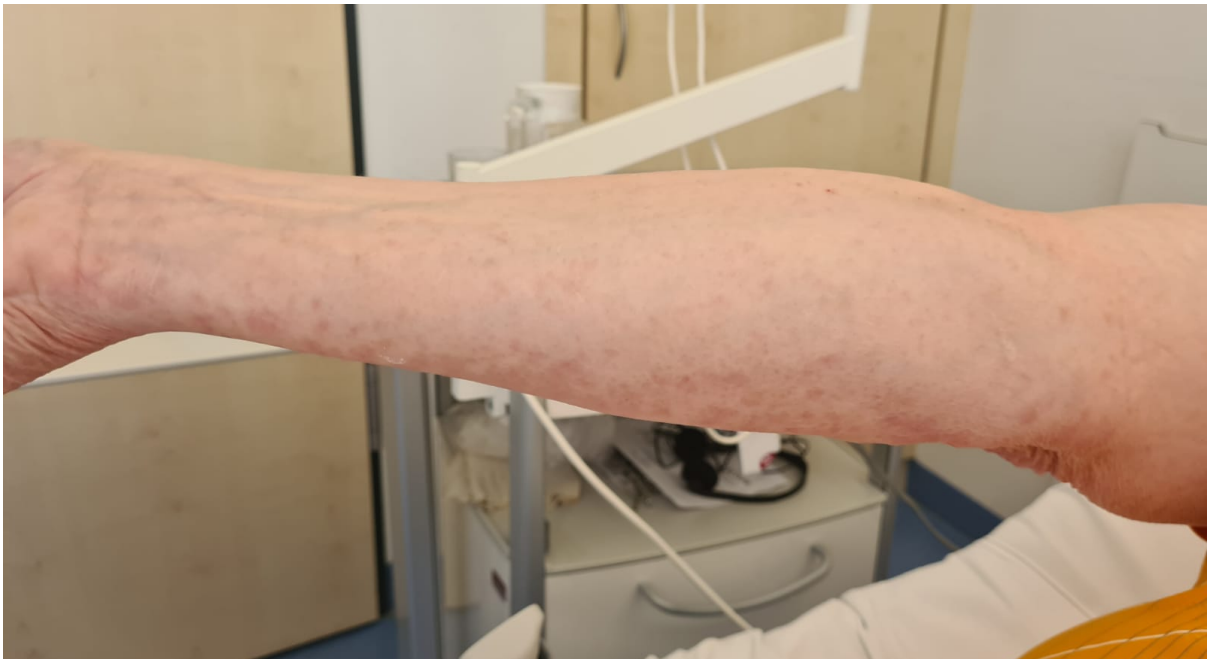
COVID-19, coronavirus disease 2019; GN, glomerulonephritis; PAS, periodic acid–Schiff; PLA2R1, M-type phospholipase A2 receptor 1; SARS-CoV-2, severe acute respiratory syndrome coronavirus type 2.

***Supplemental Figure 3*: A post-vaccinated patient with maculopapular rash and palpable purpura indicative of leukocytoclastic vasculitis before corticosteroid treatment (a) and displaying clinical improvement during treatment with corticosteroids (b).**

**a**



**b**



Case V5 gave his written consent to publish the above pictures. Detailed information on the case is provided in Supplementary Table S1.

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