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Letter to the Editor

LETTER TO THE EDITOR

Short-time interruption of second-line mycophenolate treatment in a patient with renal sarcoidosis enabled a marked antibody response to SARS-CoV-2 messenger RNA vaccine

Peter Schnuelle [1,2], Sebastian Kölling[1], Alexander Müller[1] and Wilhelm H. Schmitt[1,2]

[1]Center for Renal Diseases Weinheim, Weinheim, Germany and [2]Vth Department of Medicine, University Medical Center Mannheim, Mannheim, Germany

Correspondence to: Peter Schnuelle; E-mail: p.schnuelle@nierenzentrum-weinheim.de

Vaccine availability has contributed significantly to reducing the morbidity and mortality of the ongoing pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Patients requiring long-term immunosuppressive therapy are exposed to an increased risk [1] as they are limited in developing an adequate vaccination response. A 66-year-old male with a history of pulmonary sarcoidosis presented with severe renal function impairment in October 2020. He had received steroids for longer than 1 year until 2017. Physical examination was normal. Laboratory results revealed a serum creatinine 2.59 mg/dL, urea 97 mg/dL, creatinine clearance 28 mL/min, serum calcium 3.08 mmol/L, intact parathyroid hormone 9.1 ng/L (normal 11.3–67.0), hydroxyvitamin D 45.1 ng/mL (30–100), soluble interleukin-2 receptor (sIL-2R) 1830 U/mL (158–623), angiotensin-converting enzyme (ACE) 87.9 U/L (8.0–52.0), C-reactive protein 6 mg/L and an inconspicuous sediment with a tubular proteinuria of 263 mg/g creatinine. On ultrasound, both kidneys were of normal size and shape. A recently performed computed tomography scan ruled out hilar adenopathy or recurrent interstitial lung disease.

Based on the present findings and medical history, sarcoid interstitial nephritis was the most likely diagnosis. We decided not to do a renal biopsy because of an inherited coagulation disorder, and started with 0.5 mg/kg prednisolone. We intended to add azathioprine early because of known osteoporosis, to save steroids and because of severe kidney involvement with the risk of irreversible organ damage [2]. However, azathioprine needed to be stopped due to elevated liver enzymes. We initiated a second-line treatment with mycophenolate in January 2021. Before prescribing mycophenolate, our patient appeared somewhat under-immunosuppressed as indicated by a recurrent rise in sIL-2R. We temporarily increased prednisolone to 15 mg. He then achieved sustained stabilization of his kidney function with 5 mg prednisolone and 360 mg mycophenolic acid twice a day (Figure 1).

He received two-dose BNT162b2 vaccination on 26 March and 7 May, but had no antibody response [EUROIMMUN anti-SARS-CoV-2 ELISA assay negative for immunoglobulin G (IgG) and immunoglobulin A (IgA) on 2 July 2021]. Because of the increasing infection risk from the emerging SARS-CoV-2 delta variant, we paused mycophenolate on 9 July and administered another dose of BMT162b2 on 24 July. Subsequent antibody determination on 18 August targeting the specific SARS-CoV-2 spike protein S1 receptor binding domain with the aforementioned ELISA showed a pronounced immune response, with an IgG ratio of 9.01 and an IgA ratio of 5.18, respectively. Antibody levels are expressed as the ratio of the sample signal to a calibrator-assigned cut-off signal.

Number and type of immunosuppressive drugs are major determinants of seroconversion failure after SARS-CoV-2 vaccination [3]. In a cohort study of 404 patients with rheumatic and musculoskeletal disease, most of the non-responders were

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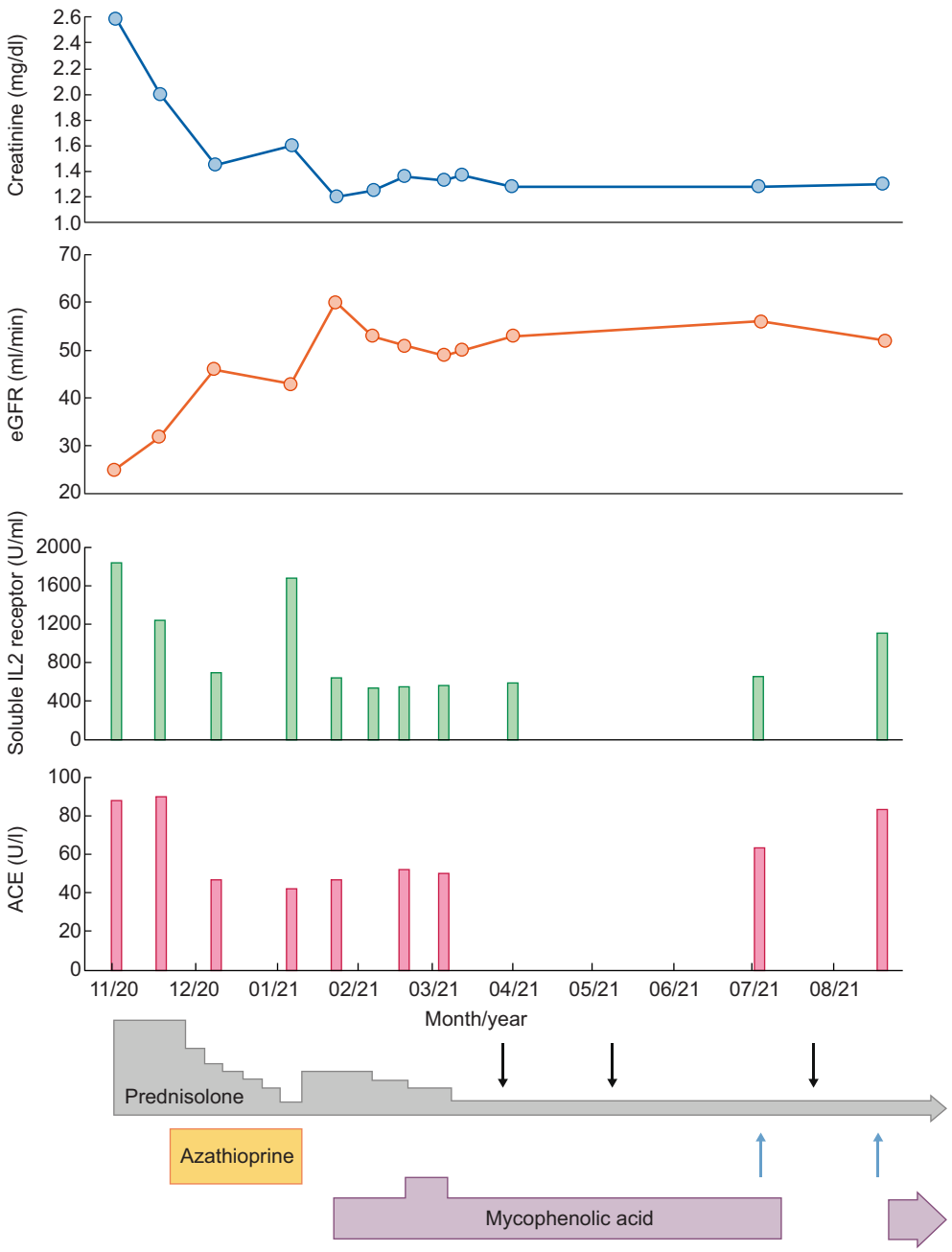

FIGURE 1: Course of renal function and disease activity during treatment. Black arrows indicate the time of the SARS-CoV-2 vaccination, blue arrows subsequent measurements of the antibody response. eGFR, estimated glomerular filtration rate.

on regimens containing mycophenolate or rituximab [4]. The level of the humoral immune response correlates with the protective effect of neutralizing antibodies [5, 6]. A recent study from New York demonstrated that positive SARS-CoV-2 antibody test results are associated with a significantly lower in-hospital mortality in coronavirus-infected patients [7]. When it became obvious that our patient had produced a marked humoral vaccine response, we continued with mycophenolate, as ACE and sIL-2R tended to rise (Figure 1). The alternative of terminating maintenance therapy had to weigh the risk of recurrent kidney disease against the inherent risks of the SARS-CoV-2 pandemic. The largest series available in sarcoid interstitial nephritis observed a high rate of 17 relapses among 47 patients (36%) during a mean treatment time of 24 months (range 1–48 months), of these, 6 in the first year [8].

In summary, short-time interruption of second-line treatment with mycophenolate enabled an adequate humoral immune response to SARS-CoV-2 mRNA vaccine without side effects. Our case adds to sparse clinical data suggesting that a temporary hold of immunosuppressive therapy may provide a feasible strategy to enhance the effectiveness of the SARS-CoV-2 vaccination in selected patients with autoimmune diseases [9].

PATIENT CONSENT

The authors declare that they have obtained consent from the patient for publication of the information about him that appears within this report.

DATA AVAILABILITY STATEMENT

The data that support the findings of this report are available from the corresponding author upon reasonable request.

CONFLICT OF INTEREST STATEMENT

None declared.

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