



Fatal SARS-CoV-2 reinfection in an immunosuppressed patient on hemodialysis

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Case presentation

A 76-year-old male with a medical history of hypertension, biological aortic heart valve replacement, and end-stage kidney disease secondary to autosomal dominant polycystic kidney disease, with a previously failed kidney transplant and on thrice-weekly in-center hemodialysis for three years, was found positive for immunoglobulin G (IgG) to SARS-CoV-2 by rapid immunochromatographic assay (BELTEST-IT COV-2, Pharmact®) in October 2020 during scheduled screening at the hemodialysis center.

The patient was asymptomatic, and the result was confirmed by chemiluminescent immunoassay (CLIA) (VITROS®). A reverse-transcription polymerase chain reaction (rt-PCR) by nasopharyngeal swab sample resulted negative. Therefore, a past asymptomatic infection was assumed, and neither treatment nor isolation was instituted.

His treatment consisted of aspirin 100 mg/day, prednisone 10 mg/day, and, until October 2019, low dose tacrolimus, on account of kidney graft intolerance and for the prevention of hyperimmunization, given the possibility of a second kidney graft.

On Christmas Eve, the patient attended a party where he was in close contact with a person later developing symptomatic COVID-19. Five days later, on December 28th, he arrived for his scheduled hemodialysis with fever, cough, and shortness of breath. An rt-PCR was positive for SARS-CoV-2, and chest computed tomography showed bilateral ground-glass opacities (Fig. 1). Hence, COVID-19 bilateral pneumonia was diagnosed, and he was admitted to the

hospital, requiring a 36% fraction of inspired oxygen to maintain an oxygen saturation of 92% or greater. At admission, laboratory tests revealed C-reactive protein (CRP) of 14.8 mg/dL (reference value < 1 mg/dL), ferritin of 1227 ng/mL (reference 20–400 ng/mL), and 8960 white blood cells per microliter with 700 lymphocytes.

IgG and IgM to SARS-CoV-2 tested negative by CLIA. The patient was initially treated with 6 mg of dexamethasone and 40 mg of enoxaparin per day. On day nine since admission, he was retested by CLIA, which detected both IgG and IgM to SARS-CoV-2.

During hospitalization, his clinical status progressively worsened, and he developed herpetic esophagitis treated with ganciclovir. Due to further deterioration of his respiratory status, on the sixteenth day, he was transferred to the ICU, and mechanical ventilation and high-dose vasopressors were needed, but, despite all efforts, he died on day 18 since admission.

Lessons for the clinical nephrologist

Human-affecting coronaviruses are known to cause reinfections. These reinfections appear to be secondary to the fact that this viral family fails to induce a long-lasting immunologic response [1].

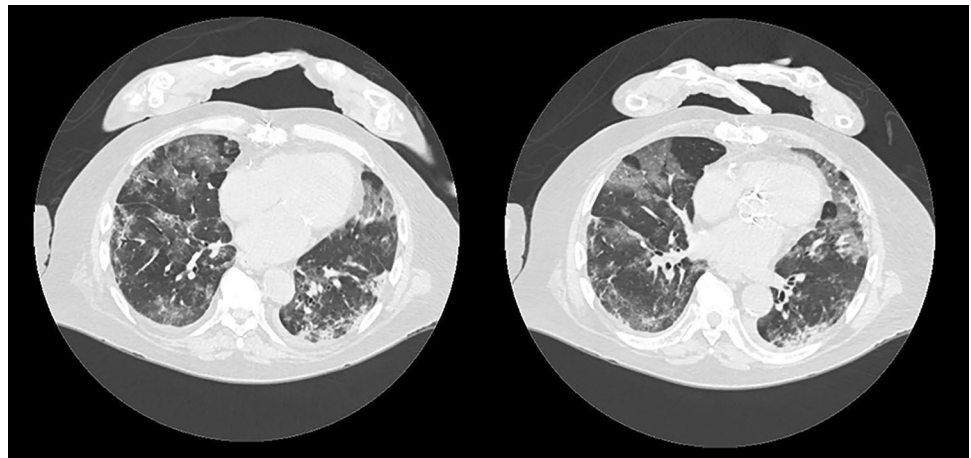
Several cases of SARS-CoV-2 reinfection have now been published, and many of them share some common features with our patient, with an initial mild or asymptomatic presentation followed by a more symptomatic or severe disease [2].

This pattern is peculiar, since in most other viral infections, reinfection appears to be milder. However, antibody titers are usually lower in non-symptomatic individuals. This is why reinfections are exceptional in patients who

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Fig. 1 Chest computed tomography showing bilateral patchy lung ground-glass opacities with lower lobe predominance



had a severe presentation [1]; exposure to higher viral loads or increased antibody production in response to the disease severity degree is probably in question [3].

There was a remarkable difference in the clinical presentation between the two episodes in the reported case, going from an utterly asymptomatic infection to a deadly one. During the first infection, the patient was tested by two different IgG and IgM tests and was only positive for IgG. The first was an immunochromatographic IgM/IgG rapid test with a sensitivity and specificity of 84.4 and 98.6%, respectively [4]. The second confirmation test was a chemiluminescence immunoassay with 94% sensitivity and 99% specificity [5]. Even though false positive rates are rare, they have been described in pregnant patients and in patients with rheumatoid factors and antinuclear antibodies [6]. Our patient did not have any of these risk factors, but the fact that we confirmed his serologic positivity with two tests makes a false positive case unlikely. The first serological result was interpreted as a sign of a previous SARS-CoV-2 infection. Conversely, at the time of reinfection, the patient no longer had detectable IgG in serum samples, while antibody response was detected on day twelve since the beginning of symptoms.

Unfortunately, we could not determine whether the difference in clinical presentation was due to a different viral strain or to a higher antibody-mediated inflammatory response at viral re-exposure. These tests are no longer in routine use, and no rt-PCR was available for the first episode.

The patient's immunological status may have played an important role, as he combined low-dose immunosuppression and dialysis-related immunodepression; indeed, end-stage kidney disease patients are known to have impaired cell function in both the innate and adaptive immune systems [7], with a low response to various vaccines (including hepatitis B virus, influenza virus, *Clostridium tetani*, *Corynebacterium diphtheria*) [8].

In conclusion, our case warns of the risk of reinfection and the risk of a severe second episode of COVID-19 in patients on dialysis and suggests that close attention for early detection of this potentially deadly occurrence should be paid in our fragile population [9].

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Declarations

Conflict of interest The authors have no conflicts of interest to declare.

Ethical approval The Local Clinical Research Ethics Committee has approved this study. Data collection has followed the Regulation (EU) 2016/679 (General Data Protection Regulation), its subordinate national and regional laws, and the Declaration of Helsinki principles.

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