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COVID-19 reinfection in a kidney transplant recipient, time for rethinking?

Reinfección por COVID-19 en un paciente portador de trasplante renal, ¿tiempo para reflexionar?

Dear Editor:

COVID-19 reinfections in immunocompromised patients are a challenge for scientific community. Here we present the first case of a kidney transplant recipient with a lethal COVID-19 reinfection.

He is a 60-year-old male, with chronic kidney disease (CKD) due to focal and segmental glomerulosclerosis that received his first kidney transplant 2004. In treatment with prednisone and rapamycin since 2007 when we was diagnosed of a hepatocellular carcinoma.

In August 2020, after a close contact to a COVID-19 family member, he developed mild symptoms (cough and low-grade fever) and SARS-CoV-2 infection was confirmed by a positive nasopharyngeal real-time reverse transcription-polymerase chain reaction (rRT-PCR) (Fig. 1). The clinical course was favorable, and he did not need further clinical assistance in that moment. A confirmatory rRT-PCR was performed showing a negative result.

In December 2020 and January 2021, he was admitted in the hospital due to two episodes of urinary tract infection

caused by *Staphylococcus aureus* and *Serratia marcescens*. In both hospitalizations, rRT-PCR were repeated five times (12th, 30th December and 4th, 9th, 17th January 2021) resulting negative in all of them. A chest X-ray performed on 12th December 2020 showed very low intensity bilateral infiltrates. In addition, on 8th January 2021, a chest-abdomen computed tomography scan demonstrated bilateral infiltrates in both hemithorax, probably as a residual lesion of the SARS-CoV-2 previous infection (Fig. 2). After diuretic and antibiotic treatment, chest X-ray improved significantly, and the patient was discharge asymptomatic 20th January 2021.

However, 28th January 2021, the patient was again admitted due to respiratory fever and acute injury of the allograft function. A chest X-ray showed bilateral infiltrates with unilateral pleural effusion. A new rRT-PCR confirmed SARS-CoV-2 infection by the same viral genotype, so immunosuppression was stopped, and dexamethasone was started. A thoracentesis of the pleural effusion demonstrated SARS-CoV-2 in the obtained sample. Antibodies (IgM and IgG) for SARS-CoV2 resulted negative. Although he was theoretically immunosuppressed, lymphocyte populations were normal. Despite

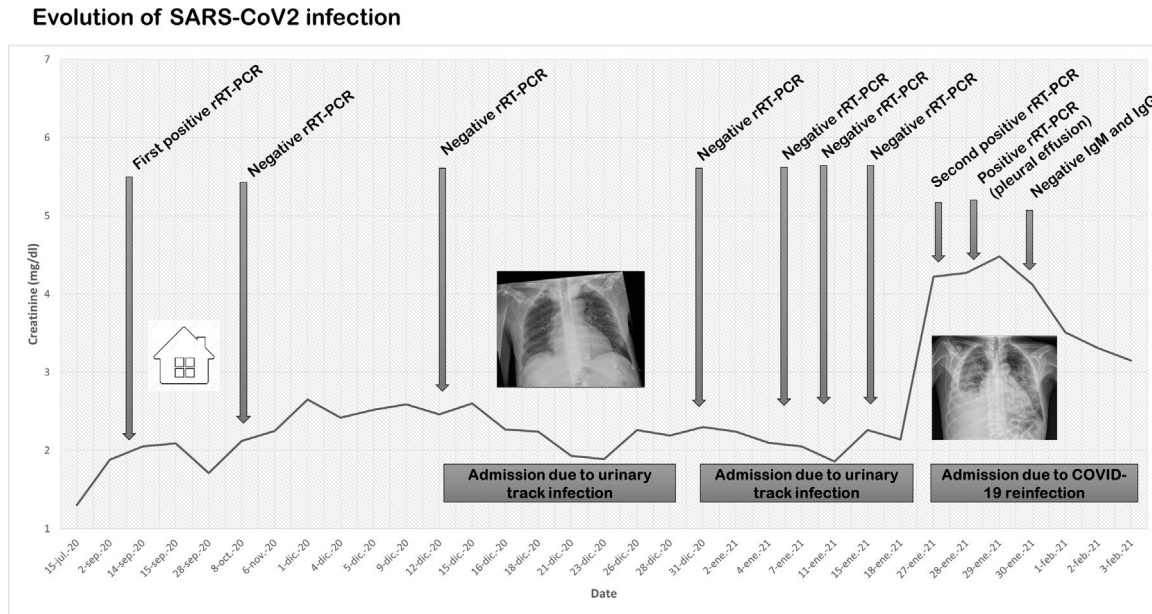


Fig. 1 – Evolution of the patient highlighting the SARS-CoV-2 tests performed since the first infection. Abbreviation: real-time reverse transcription-polymerase chain reaction (rRT-PCR).

established treatment including high flux oxygen, the patient deceased on 5th February 2021.

Several doubts have emerged around reinfections in general population. Technical errors in specimen collection or false negative results in rRT-PCR have been demonstrated in many patients driving to mistakes in COVID-19 reinfections. In addition, virus or non-active fragments of them can persist in sputum for weeks showing false positive results. However, the most part of the published reinfections have shown an asymptomatic course in the second positive rRT-PCR episode.¹ This situation interestingly differs from our patient who presented a pauci-symptomatic course of COVID-19 infection with a lethal reinfection 5 months later.

Our patient presented some confirmatory features of a COVID-19 reinfection. First, he had positive rRT-PCR concurring with a family member contact and some mild symptoms. Despite this classical clinical picture, and even using a highly specific rRT-PCR, in some circumstances false positives can occur. Second, we confirmed negative rRT-PCR in several times, but radiological images showed residual bilateral lesions suggestive of COVID-19 past infection. Third, he developed new symptoms and chest X-ray worsen significantly simultaneously. In addition, in the reinfection episode, pleural effusion revealed the presence of SARS-COV-2 in the lungs.

Reasons for reinfection have not been widely studied, in part because immune response to SARS-CoV-2 has not been yet addressed.² Probably, immunosuppressive factors can contribute to limit viral clearance and to impair cellular and humoral immunity in COVID-19 as in other infections.³ The clinical course of our patient agrees with this hypothesis. Although lymphocyte populations were normal at admission, in our patient concurred the personal history of the active neo-

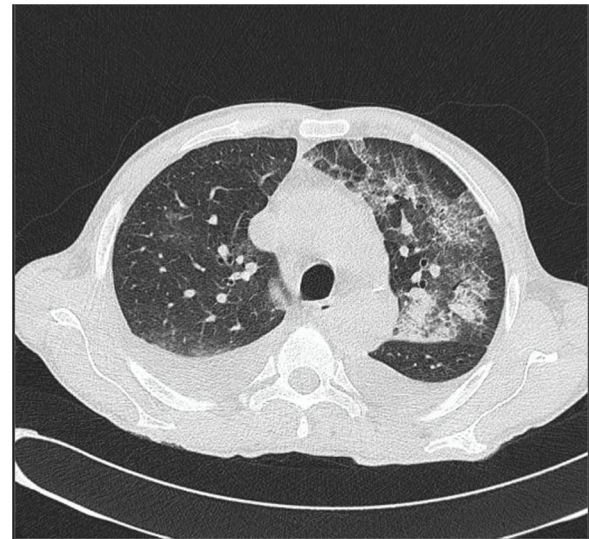


Fig. 2 – Chest and abdomen computed tomography showing bilateral infiltrates in lungs.

plasia and the immunosuppression due to kidney transplant. Unfortunately, data regarding humoral or cellular immunity was not available after the first episode.

On this regard, reinfections can raise some concerns about the COVID-19 vaccines efficacy in those populations with risk factors for attenuating humoral immunity. In addition, pivotal COVID-19 vaccines randomized clinical trials have systematically excluded CKD patients so there is an important lack of information about their efficacy in that population. A very recent investigation letter has shown that a single dose of SARS-CoV2 mRNA vaccine generates a poor antispike

antibody response, situation than can explain a COVID-19 reinfection, especially more than 4 months before the primoinfection.⁴ On the other hand, we must be cautious with those patients with prior episodes of COVID-19 who develop new symptoms and chest X-ray lesions and, of course, always recommend maintaining infection preventive measures.

In conclusion, reinfections in kidney transplants are plausible and require paying attention to those patients who developed COVID-19 symptoms even if they have had a previous episode.

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Debemos evaluar el daño renal previo en el fracaso renal agudo por COVID-19

We must evaluate the previous kidney damage in the acute kidney failure due to COVID-19

Sr. Director:

Queremos transmitir en nombre de todos los autores el agradecimiento por mostrar interés en nuestra publicación como se refleja en su carta al director^{1,2}.

Efectivamente, el tamaño muestral es una limitación de nuestro trabajo y así está reflejado en la discusión, si bien es cierto que se trata de la serie prospectiva española más amplia de fracaso renal agudo (FRA) en pacientes con COVID-19 directamente atendidos por nefrología en la fecha de la publicación. Esto supone un sesgo de selección negativo de los pacientes más críticos que precisaron una interconsulta al nefrólogo por la gravedad del cuadro, la necesidad de diálisis o las complicaciones añadidas. En ningún momento podemos tomar nuestra serie de 41 pacientes como una representación del FRA del paciente COVID en general, de hecho, nuestro planteamiento de análisis es fundamentalmente descriptivo. Nuestro enfoque es destacar la tremenda variabilidad de causas, pre-

sentaciones clínicas y desenlaces que hemos recogido y que van más allá de la afectación directa del riñón por la infección SARS-CoV-2 o por la tormenta citoquinica. Queríamos dar una perspectiva desde el punto de vista del nefrólogo, aportando claridad en un momento de grandes vacíos de información. Recuérdese que el informe COVID19 del Ministerio de abril de 2020 no reconocía la enfermedad renal crónica (ERC) como factor de riesgo, ni aportaba evidencia publicada de que el FRA fuese un problema asociado al COVID-19³.

En cuanto al diagnóstico diferencial entre FRA y ERC, ya especificábamos en el apartado de métodos que se utilizaron los criterios KDIGO para el diagnóstico del FRA. Queda aclarado en el apartado de características basales, dentro de los resultados, que nuestra población presentaba ERC de base en un 36,6%. En nuestro análisis previo sobre 1.600 pacientes ingresados en todo el hospital durante la primera ola se analiza específicamente la asociación de la ERC y del FRA de manera separada en el pronóstico de los pacientes⁴. En comentario editorial del mismo número se incide precisa-