

Conflicts of interest

The authors declare that they have no conflicts of interest.

REFERENCES

- Manns MP, Buti M, Gane E, Pawlotsky JM, Razavi H, Terrault N, et al. Hepatitis C virus infection. *Nat Rev Dis Primers*. 2017;3:17006.
- Cacoub P, Comarmond C, Domont F, Savey L, Saadoun D. Cryoglobulinemia vasculitis. *Am J Med*. 2015;128(9):950–5.
- Sethi S, Fervenza FC. Membranoproliferative glomerulonephritis—a new look at an old entity. *N Engl J Med*. 2012;366(12):1119–31.
- Santoriello D, Pullela NK, Uday KA, Dhupar S, Radhakrishnan J, D'Agati VD, et al. Persistent hepatitis C virus-associated cryoglobulinemic glomerulonephritis in patients successfully treated with direct-acting antiviral therapy. *Kidney Int Rep*. 2018;3(4):985–90.
- Obrîșcă B, Jurubiță R, Sorohan B, Iliescu L, Baston C, Bobeică R, et al. Clinical outcome of HCV-associated cryoglobulinemic glomerulonephritis following treatment with direct acting antiviral agents: a case-based review. *Clin Rheumatol*. 2019;38(12):3677–87.
- Ghosn M, Palmer MB, Najem CE, Haddad D, Merkel PA, Hogan JJ. New-onset hepatitis C virus-associated glomerulonephritis following sustained virologic response with directacting antiviral therapy. *Clin Nephrol*. 2017;87(5):261–6.
- Sollima S, Milazzo L, Peri AM, et al. Persistent mixed cryoglobulinaemia vasculitis despite hepatitis C virus eradication after interferon-free antiviral therapy. *Rheumatology*. 2016;55:2084–5.
- Chowdhury R, Tsen A. Recurrent mixed cryoglobulinemia despite sustained virologic response to treatment: a case report. *Am J Kidney Dis*. 2017;70:301–4.
- Kaegi C, Wuest B, Schreiner J, Steiner UC, Vultaggio A, Matucci A, et al. Systematic review of safety and efficacy of rituximab in treating immune-mediated disorders. *Front Immunol*. 2019;10:1990.
- Flores-Chávez A, Carrion JA, Forns X, Ramos-Casals M. Extrahepatic manifestations associated with Chronic Hepatitis C Virus Infection. *Rev Esp Sanid Penit*. 2017;19(3):87–97.
- Terrier B, Joly F, Vazquez T, Benech P, Rosenzweig M, Carpentier W, et al. Expansion of functionally anergic CD21-/low marginal zone-like B cell clones in hepatitis C virus infection-related autoimmunity. *J Immunol*. 2011;187(12):6550–63.
- Comarmond C, Garrido M, Pol S, et al. Direct-acting antiviral therapy restores immune tolerance to patients with hepatitis C virus-induced cryoglobulinemia vasculitis. *Gastroenterology*. 2017;152:2052–62.
- Mediterranean Consortium for the study of Cryoglobulinemic Vasculitis Hegazy MT, Allam WR, Hussein MA, Zoheir N, Quartuccio L, El-Khamisy SF, et al. Increased genomic instability following treatment with direct acting anti-hepatitis C virus drugs. *EBioMedicine*. 2018;35:106–13.

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Decision making – Should we perform kidney transplantation on a patient with a positive RT-PCR test for SARS-CoV-2?

Toma de decisiones - ¿Debería realizarse un trasplante de riñón a un paciente con una prueba RT-PCR positiva para SARS-CoV-2?

Dear Editor:

The COVID-19 pandemic brought new challenges to daily decision-making in Kidney Transplant (KT) Centers. Excluding infection with SARS-CoV-2 virus before patients undergo KT

became a routine due to the significant prevalence of asymptomatic infection. According to the Centers for Disease Control and Prevention (CDC), people who recovered from COVID-19 may have prolonged detection of SARS-CoV-2 RNA, without being at risk of disease transmission. Studies have indicated that patients who were hospitalized and recovered may have detectable SARS-CoV-2 RNA in the upper respiratory tract up to 3 months after symptom onset.¹ In some cases, a KT was already performed after recovery but within this timeframe.²

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Although some cases of intermittent viral shedding have been described up to 4 months after COVID-19,³ most series report a median duration of positive test of around 30 days; intermittent shedding after 2 months of symptom onset remains unlikely.³⁻⁵ Reinfection risk seems to be low,^{6,7} although reinfection with new variants must be considered.

The role of immunosuppression in COVID-19 severity is not yet fully understood. An active acute infection is generally a contraindication to KT. In a Brazilian KT center, four patients were screened for SARS-CoV-2 infection before KT and a positive result came after surgery.⁸ None of these patients developed symptoms.

We present the case of a 35-year-old patient who was admitted at our unit for a second deceased-donor (DD) KT. She had chronic kidney disease of unknown etiology diagnosed in childhood and started hemodialysis in 2005. Her first KT complicated with sepsis, primary graft dysfunction and subsequent graft nephrectomy. She maintained good adherence to hemodialysis with no major complications.

In May 2021 – after 16 years under hemodialysis – she was selected for a second DD-KT, with whom she shared the same blood type and had only 2 Human Leucocyte Antigen incompatibilities (B and DR). She was already highly immunized – Panel of Reactive Antibodies (PRA) of 44% and virtual PRA based on single antigen specificities of 99.73%. No donor specific antibodies were detected.

On admission she was asymptomatic and there was no clinical, laboratorial or radiographic sign of infection. She presented no contraindication to KT. However, she tested positive for SARS-CoV-2 on a RT-PCR test (*GeneXpert*® Ct gene E 39,2, gene N 38,9). The patient's previous history revealed a mild COVID-19 disease four months before. She was unvaccinated due to this recent infection. Antibodies to SARS-CoV-2 virus were positive, consistent with previous infection – anti-nucleocapsid 78 U/ml and anti-Spike 97 U/ml.

After discussion between the KT team and both clinical pathology and infectious disease experts the RT-PCR test was considered a false-positive due to intermittent viral shedding and the patient was accepted for KT. High-risk immunosuppression protocol with thymoglobulin 1.25 mg/kg daily for 7 days, mycophenolate mofetil 2 g daily and high dose steroids were necessary due to her increased allo-sensitization. Mycophenolate mofetil dose was reduced due to cytopenias, no dose reduction was made to other immunosuppressants. Maintenance immunosuppression included tacrolimus, mycophenolate mofetil and prednisolone.

There were no signs of respiratory infection in the post-operative period. Subsequent RT-PCR tests for SARS-CoV-2 were performed at day 8, 13 and 18 after surgery and all came negative. Antibodies titers were not repeated subsequently. The patient has currently 9 months of KT.

The risks and benefits of KT in this case were thoroughly balanced. A false-positive result was suspected due to recent infection and elevated number of PCR cycles needed to amplify viral RNA. In a young highly immunized patient under hemodialysis for 16 years it could take long before she was again selected for transplantation. However, fragile patient under immunosuppression and mild symptoms from previous COVID-19 could have been unable to build robust immune protection for a second infection with SARS-CoV-2 and the

risks of inducing immunosuppression on a patient with active COVID-19 infection could be catastrophic.

High Ct values have been frequently associated with viral shedding conditions and when interpreted with caution and integrated with other clinical signs may help some decision making, as in the present case.⁹

Urgent liver transplantation has been performed in a patient with acute liver failure, a positive RT-PCR test for SARS-CoV-2 but no respiratory symptoms.¹⁰

To our present knowledge, there is no report of a KT team deciding to perform kidney transplantation on a patient knowing he has positive RT-PCR test for SARS-CoV-2 more than 3 months after diagnosis of COVID-19. This is also the first KT on a patient with positive RT-PCR test for SARS-CoV-2 in a Portuguese transplant center.

As the number of hemodialysis patients recovering from COVID-19 grows, it is expected that this situation repeats. Kidney transplant teams should have quick access to infectious disease experts who would guide the interpretation of these screening tests in the future and help the decision to admit patients for transplant and immunosuppression.

Conflict of interest

There is no conflict of interest among all authors of this letter.

REFERENCES

1. CDC. Coronavirus Disease 2019 (COVID-19). Centers for Disease Control and Prevention; 2020 www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html
2. Murad H, Dubberke E, Mattu M, Parikh B, Wellen J, Alhamad T. Repeat SARS-CoV-2 testing after recovery. Is a pretransplant PCR necessary? *Am J Transpl.* 2021;21:3206-7, <http://dx.doi.org/10.1111/ajt.16506> [accessed 26.02.22].
3. Danzetta ML, Amato L, Cito F, Di Giuseppe A, Morelli D, Savini G, et al. SARS-CoV-2 RNA persistence in naso-pharyngeal swabs. *Microorganisms.* 2020;8:1124, <http://dx.doi.org/10.3390/microorganisms8081124>.
4. Tuan J, Spichler-Moffarah A, Ogbuagu O. A new positive SARS-CoV-2 test months after severe COVID-19 illness: reinfection or intermittent viral shedding? *BMJ Case Rep.* 2021;14:e240531, <http://dx.doi.org/10.1136/bcr-2020-240531>.
5. Sun J, Xiao J, Sun R, Tang X, Liang C, Lin H, et al. Prolonged persistence of SARS-CoV-2 RNA in body fluids. *Emerg Infect Dis.* 2020;26, <http://dx.doi.org/10.3201/eid2608.201097>. www.ncbi.nlm.nih.gov/pmc/articles/PMC741097/
6. Hansen CH, Michlmayr D, Gubbels SM, Mølbak K, Ethelberg S. Assessment of protection against reinfection with SARS-CoV-2 among 4 million PCR-tested individuals in Denmark in 2020: a population-level observational study. *Lancet.* 2021;397:1204-12, [http://dx.doi.org/10.1016/s0140-6736\(21\)00575-4](http://dx.doi.org/10.1016/s0140-6736(21)00575-4).
7. Sheehan MM, Reddy AJ, Rothberg MB. Reinfection rates among patients who previously tested positive for COVID-19: a retrospective cohort study. *Clin Infect Dis.* 2021, <http://dx.doi.org/10.1093/cid/ciab234>.
8. Viana LA, Cristelli MP, Ficher KN, Rezende JT, Villanueva LAA, Santos DWCL, et al. Kidney transplantation in patients with SARS-CoV-2 infection: a case series report. *Transplantation.* 2020;105:e1-3, <http://dx.doi.org/10.1097/tp.0000000000003521> [accessed 26.02.22].

9. Bullard J, Dust K, Funk D, Strong JE, Alexander D, Garnett L, et al. Predicting infectious SARS-CoV-2 from diagnostic samples. *Clin Infect Dis*. 2020, <http://dx.doi.org/10.1093/cid/ciaa638> [accessed 06.06.20].
10. Roupael C, D'Amico G, Ricci K, Cywinski J, Miranda C, Koval C, et al. Successful orthotopic liver transplantation in a patient with a positive SARS-CoV-2 test and acute liver failure secondary to acetaminophen overdose. *Am J Transpl*. 2020;21:1312–6, <http://dx.doi.org/10.1111/ajt.16330>.

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Online hemodiafiltration without calcium replacement using citrate as an anticoagulant and dialysis fluid with 3.5 mEq of post dilutional calcium in patients with heparin-induced thrombocytopenia: Report of 2 cases

Hemodiafiltración online sin reposición de calcio utilizando citrato como anticoagulante y líquido de diálisis con 3,5 mEq de calcio posdilucional en pacientes con trombocitopenia inducida por heparina: reporte de 2 casos



Dear Editor,

Patients with renal disease on renal replacement therapy with hemodialysis require anticoagulation of the extracorporeal system and heparin is the most common.

Heparin-induced thrombocytopenia (HIT), a serious condition, occurs in patients exposed to heparin, regardless of the dose and route of administration, with a reported prevalence of around 5%.^{1,2}

This condition is due to the development of autoantibodies against endogenous platelet factor 4 (PF4), which causes platelet activation, which in turn causes arterial and venous thrombosis in some severe cases.³

There are 2 types of HIT: type I, without significant decrease in platelet count or thrombosis; and type II, where there is thrombocytopenia with thrombosis, requiring the suspension of heparin and the use of another anticoagulant to treat thrombosis.

The presentation of HIT in hemodialysis patients motivates the search for alternatives for anticoagulation, such as the use

of predilution hemodiafiltration (HDF), continuous infusion of saline solution, use of citrate as an anticoagulant and even a change of modality to peritoneal dialysis.

The prevalence of HIT in hemodialysis patients may be up to 4%, although the presence of PF4 antibodies is higher in dialysis patients.^{4–6}

The use of citrate as an anticoagulant is common practice in continuous renal replacement therapy and requires the use of calcium replacement.⁷ There are isolated reports of the use of citrate without calcium replacement in extended dialysis in patients with acute kidney failure.⁸

Online HDF is an increasingly common hemodialysis modality in patients with chronic kidney disease (CKD). We present two clinical cases of patients with CKD on chronic hemodialysis with a history of HIT, with the use of citrate as anticoagulant implemented during online HDF without calcium replacement.

Case A. A 68-year-old male patient with a diagnosis of ANCA-p positive pauci-immune glomerulonephritis. With the progressive use of sodium heparin during dialysis sessions his platelet count decreased (Fig. 1) with positive anti-PF4, so we

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