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TRANSPLANT INFECTIOUS DISEASE

CLINICAL CORRESPONDENCE

Kidney transplantation from deceased donors with vaccine-induced thrombosis and thrombocytopenia (VITT): Definitely feasible and safe?

Daniela Picciotto | **Elisabetta Bussalino** | **Ernesto Paoletti**

Nephrology, Dialysis, and Transplantation, University of Genoa and Policlinico San Martino, Genova, Italy

Correspondence
Ernesto Paoletti, Nephrology, Dialysis, and Transplantation, University of Genoa and Policlinico San Martino, Genova, Italy.
Email: ernesto.paoletti@hsanmartino.it

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1 | INTRODUCTION

In march 2021, fatal cases of thrombosis associated with thrombocytopenia following anti-SARS-CoV2 adenoviral vaccines administration have been reported especially in younger people, the so-called vaccine-induced thrombosis and thrombocytopenia (VITT).[1]

This has raised the challenge of accepting VITT-deceased patients as organ donors, taking into account potential risks associated with transplantation, such as the occurrence of microangiopathic thrombosis of the graft, or the development of transplant-mediated alloimmune thrombocytopenia (TMA).[2]

Here, we present two cases of kidney transplantation from donors deceased as a consequence of VITT. Data on more than 1-year follow-up, the longest available, are reported.

2 | CASE REPORTS

Case 1. In early April 2021, we evaluated a 32 years old woman admitted to the Emergency Room (ER) for sudden onset of unconsciousness as a potential kidney donor. She had received the first dose of ChAdOx1-S vaccination 12 days before; her clinical history was otherwise unremarkable. Cerebral CT scan showed diffuse right intraparenchymal hemorrhage associated with extended venous thrombosis. Laboratory specimen revealed severe thrombocytopenia (platelets (PLT) count 22x10E9/L), increased D-Dimer, fibrinogen consumption, and mild anemia, whereas both hepatic and renal function were normal. After clinical brain death diagnosis and the 6 h observation period completion, we decided to perform an abdominal CT scan to rule out the presence of renal vein thrombosis, and a kidney biopsy with the aim of excluding microangiopathic thrombosis. The TC abdomen scan showed normal kidney structure and perfusion. The kidney biopsies showed tubular necrosis and neither microangiopathic lesions nor glomerular lesions (Figure 1). Consequently, the patient was considered an eligible kidney donor. Liver and lungs were also judged suitable for donation, and the organs were allocated in other centers. The liver recipient had an unremarkable postoperative course with a good and immediate graft function. Table 1 depicts clinical data of the two kidney recipients (R1 and R2).

Case 2. When the knowledge of VITT and its clinical management were undoubtably improved, we evaluated, as a potential kidney donor, an 18 years old woman with no relevant medical history, who received her first dose of ChAdOx1-S vaccination a week before. She was admitted at the ER because of headache and the onset of leg paresthesia.

CT scan showed venous thrombosis and cerebral hemorrhage, the blood count revealed moderate thrombocytopenia (PLT90x10E9/L). Thrombotic thrombocytopenic purpura was ruled out (ADAMTS13 in normal range; no schistocytes in the peripheral blood smear), and few days later the diagnosis of VITT was confirmed by detection of positive anti-platelet factor 4 antibodies (anti-PF4 Ab). In the meanwhile, the patient was admitted to the Intensive Care Unit, and treatment for a suspected case of VITT consisting of intravenous immunoglobulins (IVIG), steroids, and anticoagulation with bivalirudin was started. Few

Abbreviations: ATG, anti-thymocyte globulin; BPR, biopsy-proven rejection; DGF, delayed graft function; DSA, donor-specific antibodies; ECDs, expanded-criteria donors; ER, emergency room; ITP, immune thrombocytopenic purpura; IVIG, intravenous immunoglobulins; MM, mismatches; PF4, platelet factor 4; PLT, platelets; PRA, panel-reactive antibodies; TMA, transplant-mediated alloimmune thrombocytopenia; VITT, vaccine-induced thrombosis and thrombocytopenia.

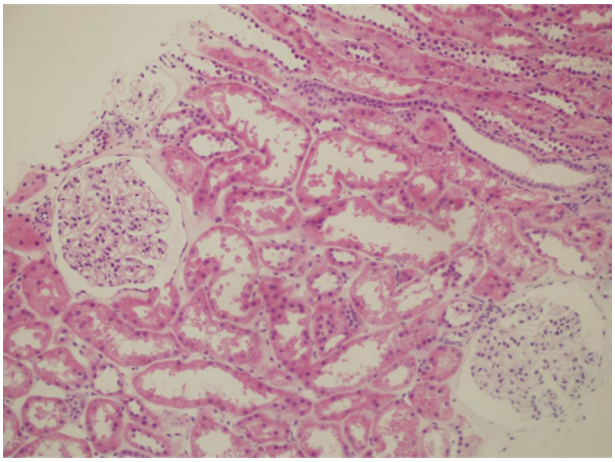

FIGURE 1 Preimplantation graft biopsy of the first vaccine-induced thrombosis and thrombocytopenia (VITT) donor showing acute tubular injury with blebbing, flattened epithelium, and dilated lumen; normal glomeruli; no signs of micro- or macrothrombosis.

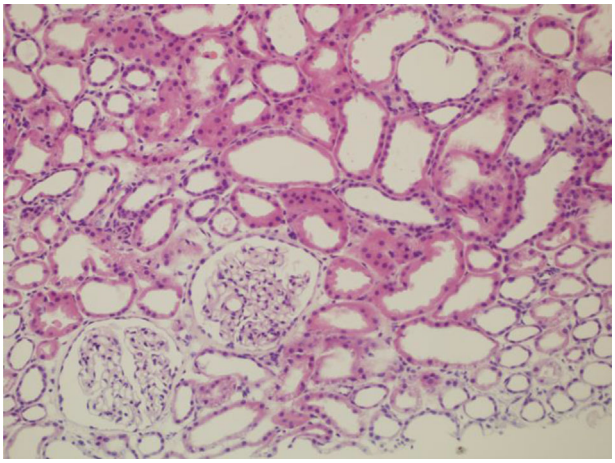

FIGURE 2 Preimplantation graft biopsy of the second vaccine-induced thrombosis and thrombocytopenia (VITT) donor showing diffuse acute tubular injury with flattened epithelium and focal cellular detachment; normal glomeruli; no signs of micro- or macrothrombosis

days later her neurological conditions worsened, and a clinical brain death diagnosis was made. The patient was considered as a potential transplant donor, and bivalirudin was continued in order to preserve the organs to engraft. Total body CT scan did not show splanchnic or renal vein thrombosis, and renal biopsies ruled out macro- or microthrombosis, showing features of acute tubular necrosis without signs of glomerular or vascular damage in both kidneys (Figure 2). Heart, lungs, liver, and kidneys were judged all suitable for organ donation with acceptable risk according to a hematologist second opinion. Close monitoring of anti-PF4 Ab in the two kidney recipients was performed every 72 h until discharge and always tested negative. Of note the liver recipient engrafted in another transplant center developed thrombocytopenia with anti-PF4 Ab positivity and was therefore treated with steroids, IVIG and fondaparinux with a progressive reduction of the antibody titre and full negativization after 7 months. Moreover, an increase in liver enzymes, still under investigation, was reported at last follow-up. Table 1 shows clinical characteristics of our two kidney recipients (R3, R4).

2.1 | Follow-up

During a 1 year follow-up period, we did not observe hematological complications in all kidney transplant recipients. R1 showed transient deterioration of kidney function after 2 months from transplantation, but the allograft biopsy was unremarkable. Graft function then remained stable throughout the entire follow-up.

R2 had an immediate graft function and did not develop any complication during follow-up.

Regarding the two kidney recipients from the second VITT donor, both showed an overall unremarkable clinical course after transplantation. Interestingly, the cause of end stage kidney disease of R3 was

TABLE 1 Clinical characteristics of the four kidney recipients and postoperative hematological follow-up

	Gender	Age	Nephropathy	DSA	Number of MM	PRA%	Induction therapy	Postoperative thrombotic or hemorrhagic events	PLT count at trans-plantation (x10E9/L)	Lowest PLT count (x10E9/L)	PLT at discharge (x10E9/L)	Anti-PF4 Ab
R1	F	52	Chronic glomeru-lonephritis	0	4	0	Basiliximab	0	397	209	492	n.a.
R2	F	20	Frasier syndrome	0	4	0	Basiliximab	0	337	190	233	n.a.
R3	M	41	Hypertensive proteinuric nephropathy	0	4	0	ATG	0	132	91	184	0
R4	M	48	IgA nephropathy	0	4	0	ATG	0	277	193	428	0

Abbreviations: anti-PF4 Ab, anti-platelet factor 4 antibodies; ATG, anti-thymocyte globulin; DSA, donor-specific antibodies; MM, mismatches; PLT, platelets; PRA, panel-reactive antibodies.

TABLE 2 Kidney allograft function follow-up

	DGF	Creatinine (mg/dl) nadir	Creatinine (mg/dl) at last follow-up	Proteinuria (g/24 h) at last follow-up	DSA at 6 months	For cause biopsy	BPR
R1	0	1.0	1.2	0.19	0	1	0
R2	0	1.1	1.1	0.1	0	0	0
R3	0	1.4	1.5	0.32	0	0	0
R4	0	1.3	1.4	0.17	0	0	0

Abbreviations: BPR, biopsy-proven rejection; DGF, delayed graft function; DSA, donor-specific antibodies.

a thrombotic microangiopathy secondary to malignant hypertension, with a negative genetic testing for hemolytic uremic syndrome and normal ADAMTS13. Consequently, complement proteins C3 and C4 as well as haptoglobin concentration were monitored for 15 days after kidney transplantation, and no alterations were observed. Finally, R4 was hospitalized shortly after transplantation due to an episode of acute pyelonephritis related to *Pseudomonas aeruginosa* infection, but no other complications occurred until now (Table 2).

3 | DISCUSSION

Accepting VITT-deceased donors was a very difficult dilemma to face for the transplant community.

Although the great majority of kidney transplants from VITT donors was successful, one of the two recipients from the first reported VITT donor developed DGF and preimplantation biopsies showed multiple thrombi within the glomerular capillaries,[3] whereas an early allograft dysfunction for a major thrombotic complication needing explantation and signs of thrombotic microangiopathy in two pretransplant allograft biopsies with subsequent DGF in one recipient were reported in two series from UK and France.[4,5]

Last, a retrospective analysis from the Eurotransplant International Foundation reported two thrombosis correlated complications.[6]

In summer 2021 targeted guidelines for the assessment of VITT organs and the decision making process leading to donation were released,[7] emphasizing the need of accepting VITT-deceased donors with extreme caution and only after rigorous assessment of organ functionality and coagulation tests.

Even before guidelines were released, we decided to perform preimplantation biopsies with the intent of excluding donation in case of signs of microangiopathy or thrombotic involvement of the organ, but this *caveat* was not attended in other transplant centers possibly leading to disappointing results.

Moreover, it is of utmost importance to perform a strict and prolonged monitoring of the recipients bearing in mind that both the graft function of the liver and kidney recipients of the second VITT deceased donor is good but not fully satisfactory at last follow-up despite the young age of the donor, the acceptable preimplantation biopsy, and the good immunological matching.

Indeed, our study is the first to report a more than 1-year follow-up of kidney recipients from VITT deceased donors.

Last, what we have learned with the VITT experience could be easily translated in case of immune thrombocytopenic purpura (ITP)-deceased donors, although TMA, in analogy to what was recently observed with VITT cases,[8] is uncommon in kidney transplantation compared to liver transplantation due to a lower passenger lymphocyte burden.[9]

This is of relevance taking into account that the currently and worldwide used mRNA-based anti-SARS-CoV-2 vaccines were not associated with VITT occurrence, whereas both cases of de novo and of exacerbation of preexisting ITP were reported.[10]

In conclusion, kidney donation from deceased VITT patients seems to be safe in terms of patient and graft survival. Nevertheless, it is of utmost importance to assess eventual micro and macroscopic thrombotic damages in the graft and to apply a strict and prolonged follow-up for recipients.

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CONFLICT OF INTEREST

The authors of this manuscript have no conflict of interest to disclose as described by the Transplant Infectious Disease.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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