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Solid organ procurement and transplantation from deceased donors with vaccine-induced thrombosis and thrombocytopenia

To the Editor:

In late February 2021, the first cases of vaccine-induced thrombosis and thrombocytopenia (VITT) were observed in patients after immunization with the ChAdOx1 nCoV-19 adenoviral vector vaccine (Oxford, AstraZeneca) against SARS-CoV-2.[1] This prothrombotic response is presumed to be mediated by anti-platelet factor 4 (PF4) antibodies that activate platelets and induce activation and extracellular trap formation of neutrophils.[2] These antibodies can also be seen in autoimmune heparin-induced thrombocytopenia, but all the described cases had no previous exposure to heparin.[1] As of June 21, 2021, more than 4.2 million people have received a first dose of the ChAdOx1 nCoV-19 adenoviral vector vaccine in France (https://ansm.sante.fr/). From the beginning of April 2021, the French National Organ Procurement Agency (https://www.agence-biomedecine.fr/) was alerted by the identification of potential deceased donors with clinical and biological features consistent with VITT. Given the global decrease in transplant activity during the COVID-19 pandemic[3] and the setting up of a worldwide vaccination strategy, these new cases challenged the procedure of organ procurement and transplantation, due to the possible extensive thrombosis in organs[4] and also transmission of VITT to the recipients.[5] Here, we report the first use and outcome of solid organ transplant procured from donors who died of complications from VITT.

From April 9 up to May 7, 2021, we identified five potential deceased donors with VITT, using existing diagnostic criteria[1] with confirmation by hematologist evaluation. All the patients had received the ChAdOx1 n-CoV-19 adenoviral vector vaccine at a median of 13 days (range, 8–14 days) prior to intensive care unit admission. Four patients presented with cerebral venous thrombosis. All presented thrombosis in other sites, intracranial hemorrhage and thrombopenia (Table 1). Two organ procurement procedures were canceled (one due to family refusal and the other because of severe disseminated intravascular coagulation). Three organ procurement procedures were achieved. During these ones, two livers were discarded because of extensive portal vein thrombosis and one lung required a thrombectomy for segmental pulmonary embolism. Finally, 10 organs (six kidneys, two hearts, one lung, and one liver) were recovered and transplanted to nine recipients, who were followed until June 21, 2021 (Table 1).

After a median follow-up of 52 days (range, 16–77 days), all recipients were alive with adequate functioning transplants. Patients experienced neither severe thrombotic nor hemorrhagic event. Two kidney transplant recipients displayed delayed graft function (including one showing glomerular microthrombi on preimplantation biopsy), that finally gradually recovered. One kidney transplant recipient underwent a biopsy at 10 days posttransplant showing mild interstitial inflammation and tubulitis, unrelated to VITT, which was treated by steroid pulses, with good subsequent function. Only one recipient displayed thrombocytopenia, but was present before transplantation and secondary to hepatic cirrhosis. To date, no recipient had detectable anti-PF4 antibodies (tests performed at a median of 10 days posttransplant) and eight have been discharged from hospital (Table 1).

This report summarizes the outcomes of organ procurement and transplantation from deceased donors with VITT in France. The potential risks were to transplant organs with thrombosis (as in the case of disseminated intravascular coagulation[4]), which could compromise organ function, and/or transmitting the systemic disease to the recipient.[5] To mitigate these risks, the French National Organ Procurement Agency immediately provided guidelines for the screening, procurement, and transplantation from such donors, as well as recipient monitoring (the detailed protocol is provided in the Supplementary Material). These guidelines led to the following: (1) a donation procedure was canceled in the case of severe disseminated intravascular coagulation; (2) organs were extensively assessed for the presence of thrombi (including biopsy if required) and discarded if thrombi were extensive; (3) after transplant, recipients underwent serial monitoring of thrombotic/hemorrhagic events, hemostasis, and anti-PF4 antibodies. Our analysis shows that the early outcomes of these transplants were favorable. While the presence of thrombi in a few organs suggests the possibility that organ function could be compromised if thrombosis was extensive, we were able to select organs with limited thrombi and did not find any evidence of transmission of VITT to the recipients. In conclusion, our data support that organs from deceased donors with VITT may be suitable for transplantation and should be carefully assessed, but not systematically discarded.

TABLE 1 Characteristics of the five deceased donors with vaccine-induced thrombosis and thrombocytopenia (VITT) screened for organ donation and the nine related transplant recipients

Organ donors	Donor A	Donor B	Donor C	Donor D	Donor E
Type of donation	Donation after brain death	Donation after brain death	Donation after circulatory death	Canceled (family refusal)	Canceled (severe disseminated intravascular coagulation)
Age (years)	41	69	67	60	66
Sex	Male	Female	Male	Male	Female
Time from vaccination to admission (days)	14	10	13	13	8
Time from vaccination to death (days)	17	12	16 (limitation of therapeutic efforts)	17	9
Preexisting conditions	Cerebral aneurysms, hypertension, pericarditis, pneumothorax	Hypertension, migraines	Hypertension, stroke, sleep apnea syndrome	Type 2 diabetes, hypertriglyceridemia, atrial extrasystoles	Hypertension
Medication on admission	Antihypertensive agent	Antihypertensive agents, analgesics, triptans	Antihypertensive agent, antiplatelet therapy	Oral hypoglycemic agent, fibrate, beta-blocker	Antihypertensive agent
Cerebral venous (sinus) thrombosis	Yes	Yes	No	Yes	Yes
Splanchnic vein thrombosis	Yes	No	Yes	Yes	Yes
Pulmonary embolism	Yes	Yes	No	No	No
Other thrombosis	No	No	No	No	Adrenal vein
Intracranial hemorrhage	Yes	Yes	Yes	Yes	Yes
Lowest platelet count prior to donation (giga/liter)	41	6	37	11	31
D-dimer peak (ng/ml)	>20 000	>20 000	> 20 000	> 20 000	> 20 000
Anti-PF4 antibodies (optical density)	Positive (2.6)	Positive (2.17)	Negative	Positive	Positive

(continues)

TABLE 1 (Continued)

Recipients	A1	A2	A3	B1	B2	B3	B4	C1	C2	–	–
Transplanted organ(s)	Heart	Left kidney	Right kidney	Heart and liver	Lungs	Left kidney	Right kidney	Left kidney	Right kidney	–	–
Age (years)	54	40	46	64	58	52	70	67	68	–	–
Sex	Male	Female	Male	Male	Female	Male	Male	Male	Female	–	–
Postoperative thrombotic event	No	Glomerular microthrombi on preimplantation biopsy	No	No	Pulmonary embolism (inherited from donor)	No	Glomerular microthrombi on preimplantation biopsy	No	No	–	–
Postoperative hemorrhagic event	No	Peri-graft hematoma	No	No	No	No	No	No	No	–	–
Lowest postoperative platelet count (giga/liter)	130	207	100	120	465	Pending	87, thrombo-cytopenia present before transplantation (cirrhosis)	164	200	–	–
Anti-PF4 antibodies	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	NA	–	–
Graft outcome	Functional	Functional	Functional	Functional	Functional	Functional	Delayed graft function (recovered)	Delayed graft function (recovered)	Functional	–	–
Patient outcome	Alive, discharged from hospital at day 52 posttransplant	Alive, discharged from hospital at day 16 posttransplant	Alive, discharged from hospital at day 10 posttransplant	Alive	Alive, discharged from hospital at day 54 posttransplant	Alive, discharged from hospital at day 28 posttransplant	Alive, discharged from hospital at day 15 posttransplant	Alive, discharged from hospital at day 23 posttransplant	Alive, discharged from hospital at day 16 posttransplant	–	–

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clinical research/practice, donors and donation, donors and donation: deceased, organ procurement and allocation

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DISCLOSURE
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