Living kidney transplantation without perioperative anticoagulation therapy for a patient with heparin-induced thrombocytopenia

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Introduction: Heparin-induced thrombocytopenia is an antibody-mediated acquired prothrombotic state induced by heparin exposure. The risk of thromboembolic diseases in kidney transplantation with heparin-induced thrombocytopenia without perioperative anticoagulation has not been determined.

Case presentation: A 64-year-old male hemodialysis patient with heparin-induced thrombocytopenia was referred to our hospital for living kidney transplantation. Anti-heparin-induced thrombocytopenia antibody was positive at the time of referral; however, it turned negative 4 months after heparin cessation during hemodialysis sessions. Living kidney transplantation by donation from his wife was performed using the standard technical procedure. Both heparinization and application of medical equipment containing heparin were avoided; however, no anticoagulant was administered intra- and postoperatively. The graft kidney functioned immediately, and no thromboembolic event related to heparin-induced thrombocytopenia occurred.

Conclusion: Kidney transplantation without perioperative anticoagulation therapy after disappearance of anti-heparin-induced thrombocytopenia antibody is a well-tolerated treatment option for patients with end-stage kidney disease.

Key words: end-stage renal disease, heparin, heparin-induced thrombocytopenia, kidney transplantation.

Keynote message

KTx without perioperative anticoagulation therapy is a well-tolerated treatment option for end-stage kidney disease patients with past history of HIT after disappearance of anti-HIT Ab.

Introduction

HIT is an Ab-mediated acquired prothrombotic state induced by heparin exposure. The risk of HIT was reported in approximately 3% of patients who received heparin exposure.1 While some cases of HIT in KTx were reported, the risk of thromboembolic diseases in KTx with HIT has not been determined.2–6 There were a few case reports on successful KTx in patients with a history of HIT; however, these patients received anticoagulants, although it is not required during typical KTx.4–6 We report a case of successful living KTx without perioperative anticoagulation in a patient with end-stage renal disease with a history of HIT.

Case presentation

A 63-year-old male patient with end-stage renal disease was referred to our hospital for living KTx by donation from his wife. He started HD 2 months before being referred to our hospital. Initially, unfractionated heparin was infused as anticoagulant during HD; however, clotting in the dialysis membrane had frequently occurred, and thrombocytopenia had been gradually exacerbated (Fig. 1). Serum anti-HIT Ab level was examined for the suspicion of
HIT, and seropositivity of anti-HIT Ab led to the diagnosis of HIT type II. Unfractionated heparin was discontinued and changed to argatroban as the anticoagulant during HD. Thrombocytopenia gradually improved, and events of clotting in the HD membrane also decreased after changing the anticoagulant. Negative conversion of serum anti-HIT Ab was confirmed 4 months after unfractionated heparin cessation. Preservation of seronegative status and absence of thrombotic complications were confirmed by enhanced CT, and then, living KTx between spouses was performed. Maintenance HD therapy and three-time DFPP against flowcytometry B-cell crossmatch positivity due to the presence of donor-specific anti-HLA Ab (mean fluorescence intensity was 1156) were conducted before KTx using argatroban. Both heparinization and application of medical equipment containing heparin were avoided during the operation. No anticoagulant was administered even during vessel suturing. The graft kidney functioned immediately, and maintenance HD was withdrawn (Fig. 2). No thromboembolic adverse event has occurred, and graft function is well-maintained 1 year after transplantation.

**Discussion**

Almost all HD patients are exposed to heparin, which is used as an anticoagulant during each treatment session, and chronic intermittent heparin exposure is associated with developing anti-heparin Ab, which is observed in approximately 10% of these patients.7 Although there is a high prevalence of anti-heparin Ab in HD patients, thromboembolic complications with thrombocytopenia do not always develop even in this status.7 The pretest probability of HIT uses the four T’s scoring system: degree of thrombocytopenia, timing of thrombocytopenia with respect to heparin exposure, occurrence of thrombotic complications, and absence of alternative explanations for thrombocytopenia.5,8 Our patient did not present with systemic thromboembolic complications but had clotting in the dialysis membrane and more than 50% platelet count fall after heparin exposure without other detectable causes of thrombocytopenia. Both the presence of anti-heparin Ab with these typical clinical symptoms and recovery of thrombocytopenia after replacement of unfractionated heparin with argatroban support the diagnosis of HIT type II in this case.

We found 10 cases of HIT in KTx3–6,9–14 (Table 1). Seven of the 11 patients were diagnosed preoperatively on the basis
of the thrombotic complications, while four patients were diagnosed during or after transplantation. All four patients who had not been diagnosed before transplantation and one patient who underwent a successful retransplantation after an initial HIT with graft loss developed thrombotic complications requiring anticoagulation therapy after KTx. Two of the five patients lost graft function due to thrombosis. Six patients diagnosed as having HIT before transplantation did not develop thrombotic complications except for one patient with antiphospholipid Ab syndrome.11 The anti-HIT Ab titer never developed thrombotic complications except for one patient who underwent a successful retransplantation after an initial HIT with graft loss. Recurrence19 KTx without anticoagulants may be considered for recipients who are diagnosed with HIT without systemic thromboembolism. Lastly, non-heparin anticoagulant was considered to potentially facilitate perioperative bleeding. Argatroban is the only drug approved by Japanese health insurance as an anticoagulant for patients with HIT. No specific antidote is available for argatroban, and thus continuous administration of argatroban during the peritransplant period may make it difficult to control sudden massive bleeding. On the other hand, this is only a single case report. Further investigation including prospective large-sized clinical studies is required to establish anticoagulant management in KTx of patients with HIT.

We successfully performed living KTx without perioperative anticoagulation in a patient with HIT. KTx without perioperative anticoagulation after disappearance of anti-HIT Ab could be a well-tolerated treatment option for patients with end-stage kidney disease.

**Author contributions**

Nishida H contributed to the conception of the work, the acquisition, analysis, and interpretation of data for the work. The author drafted the article. Fukuhara H, Yamagishi A, Hosoya N, Ichiyanagi O, Sakurai T, Naito S, Kawazoe H, Ymanobe T, Kato T, and Tsuchiya N contributed to the analysis and interpretation of data for work. The authors revised the article critically for important intellectual content. All the authors agreed to be accountable for all aspects of the work in ensuring the questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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**Table 1** Review of literature on KTx with HIT

| Organ                  | Case         | Diagnosis of HIT | HIT Ab at KTx | Anticoagulant therapy during operation | Thrombotic complication | Author       | Year  |
|------------------------|--------------|------------------|---------------|--------------------------------------|-------------------------|--------------|-------|
| Kidney                 | 19 years old male | After KTx        | N/A           | Heparin                              | TMA in transplanted kidney | Anderegg BA  | 2005  |
| Kidney                 | 17 years old male  | Before KTx       | Negative      | Recombinant hirudin                  | None                    | John U       | 2006  |
| Kidney                 | 22 years old female | After KTx        | N/A           | Heparin                              | Thrombosis from IVC to EIV and PE | Dracopoulos S | 2007  |
| Kidney                 | 68 years old male  | After KTx        | N/A           | Heparin                              | DVT and PE              | Maldonado A  | 2009  |
| Kidney                 | 50 years old male  | Before KTx       | Negative      | Coumadin                             | DVT and PE              | Muzaffar M   | 2012  |
| Kidney                 | 67 years old female | During KTx       | N/A           | Darbogaran                           | DVT                     | Sakakibara S | 2014  |
| Kidney                 | 23 years old female | Before KTx       | N/A           | Bivalirudin                          | None                    | Podolak B    | 2014  |
| Kidney                 | 64 years old female | Before KTx       | Negative      | None                                 | None                    | Our case     | 2019  |
| Kidney                 | 36 years old female | Before KTx       | Negative      | Darbogaran                           | None                    | Jozwik A     | 2018  |
| Pancreas and kidney    | 58 years old female | Before KTx       | Negative      | Argatroban                           | None                    | Taguchi K     | 2019  |
| Heart and kidney       | 49 years old female | Before KTx       | Positive      | Bivalirudin                          | None                    | Choxi AA      | 2017  |
Kidney transplantation for a HIT patient

Ethics approval and consent to participate

According to the Ethical Guidelines for Medical and Health Research involving Human Subjects in Japan, ethical approval is not required for case reports.

Consent for publication

Written informed consent was obtained from the patient for the publication of this case report and any accompanying test results.

Conflict of interest

The authors declare no conflict of interest.

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