CASE REPORT

Live kidney donation from a person with haemophilia

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SUMMARY

There are many documented cases of a person with haemophilia successfully receiving a solid organ transplant, including liver and kidney. However, there is no literature reporting live organ donation by a person with haemophilia. Presumably, this is because the associated risks of excessive bleeding, inhibitor development after a period of intensive treatment with factor replacement and the possibility of variant Creutzfeldt-Jakob disease transmission in those previously treated with blood products, are considered excessive. This case describes a 24-year-old man who was diagnosed with mild haemophilia A during his pretransplant work up as a potential live kidney donor to his sister. He then went on to successfully donate his kidney, without complications. To the best of our knowledge, this is the first description of a person with haemophilia being a living organ donor.

BACKGROUND

In this case, a diagnosis of mild haemophilia A was made during work up for a live kidney donation.^{1 2} It highlights the importance of taking a detailed bleeding history as well as referring for specialist haemostasis investigation when the bleeding history and coagulation screen suggest a possible bleeding disorder. In this case, surgery was able to proceed with minimal delay due to careful planning and a multidisciplinary approach. The case is notable as the first description of a person with haemophilia being a living organ donor.

CASE PRESENTATION

A 24-year-old man volunteered to donate a kidney to his 30-year-old sister who had end-stage renal disease secondary to diabetic nephropathy. The potential donor had an excellent renal function, no significant medical history and was not on any medications. His assessment was entirely satisfactory with the exception of a prolonged activated partial thromboplastin time (APTT) of 36 s (normal range 23.4–32.4). The prothrombin time was normal.

A detailed bleeding history was taken. The patient reported episodes of prolonged bleeding including a cut on his chin that bled for over 12 h, nosebleeds lasting for longer than 30 min and extensive bruises out of keeping with the injury that caused them. Most significantly, he also reported persistent bleeding for 1 week after a dental extraction. There was no family history of a bleeding disorder. In addition to his sister, there were two brothers also. He was referred to the

Northern Ireland Haemophilia Comprehensive Care Centre for further investigation.

INVESTIGATIONS

The prolonged APTT was found to correlate with 50:50 mixing studies. Factor VIII levels showed a discrepancy between the one-stage and chromogenic assays. Both methods were used as, in the Northern Irish population, there is a common mutation that gives rise to lower results being obtained with the chromogenic assay.³ Unusually, however, the discrepancy was the opposite of what is usually observed, in that the one-stage showed levels of factor VIII to be low at 0.14 IU/mL, while the chromogenic assay gave a higher result of 0.55 IU/mL (normal range 0.6–1.3 IU/mL). This was in keeping with mild haemophilia A. Von Willebrand antigen and activity levels were normal. Mild haemophilia is often diagnosed later in adulthood as opposed to severe haemophilia, which is detected in infancy due to its more overt bleeding symptoms.

Following genetic analysis, the c.5123G>A p. Arg1708His mutation was identified. This mutation is associated with mild haemophilia A. The donor's two brothers were tested and found to have the same factor VIII assay results and mutation. This mutation has not had a previously reported inhibitor risk.

TREATMENT

The potential complications of a person with haemophilia as an organ donor were discussed at an interspecialty multidisciplinary meeting. Aside from the diagnosis of mild haemophilia A, the donor had no other medical history. It was agreed that supportive treatment with recombinant factor VIII would allow the donor's factor VIII level to be maintained at a haemostatic level throughout the perioperative period. The patient was counselled regarding the potential risks of surgery, including uncontrolled bleeding and the possibility of developing an inhibitor to factor VIII after a period of intensive treatment. A discussion also took place in relation to how best to replace the factor VIII. Given the potential fluid balance issues, desmopressin acetate was considered to be inappropriate. Monitoring during the perioperative period, therefore relied on results from the one-stage assay and for this reason a recombinant factor VIII product, which is measured by the one-stage assay, was chosen for replacement.

Of note there were no other potential live donors and the recipient's overall health remained

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poor on maintenance dialysis therapy. The donor was very keen to proceed and, following informed consent, he was admitted for a laparoscopic nephrectomy.

Four thousand units of recombinant factor VIII were administered 1 h preoperatively and titrated twice daily to ensure that a trough level of 100% was maintained throughout the perioperative period and postoperative period. Once the kidney had been removed, tranexamic acid was started intravenously during the operation, and continued orally thereafter for a total of 14 days. The patient's postoperative course was uneventful and he was discharged after 7 days.

DISCUSSION

For suitable patients with end-stage renal disease, transplantation is the optimal form of renal replacement therapy, with enhanced quality and quantity of life. Transplantation from a live donor kidney is associated with superior graft and patient survival compared to that from deceased donor kidneys. In the UK, between April 2012 and March 2013, more than one-third of all renal transplants (1068) were from live donors.⁴ Although this is now a routine practise, exposing a healthy person to short-term and long-term risks for a procedure that has no direct physical benefit for them requires vigilance and careful consideration. The welfare of the donor remains paramount at all times.

In the UK, the morbidity rate after laparoscopic nephrectomy in healthy donors is reported as 4.5%, with a bleeding complication rate of 0.45%.⁵ Current guidelines advise that 'all donors should have a full blood count and clotting screen as part of their assessment', but they do not offer particular advice in regard to haemophilia.⁶ If the history raises concerns of abnormal haemostasis and the coagulation screen is abnormal, then referral should be made for specialist haemostasis investigation even in patients with no known personal or family history of bleeding disorder—as in this case. It is possible to have a bleeding disorder with a normal coagulation screen result and so a detailed bleeding history should always be taken regardless of the results of coagulation screen tests.

Haemophilia A is an X linked recessive disorder characterised by a deficiency in factor VIII levels. Assays commonly used to measure factor VIII do so indirectly by measuring its activity in generating factor Xa. In most cases of haemophilia A, the one-stage and chromogenic assays will give equivalent results, but in some cases there will be a discrepancy between assays. A common discrepancy in the Northern Irish population is to have a lower result with the chromogenic assay. In this case, the reverse was true, with the chromogenic assay giving the higher value. This highlights the importance of carrying out both the one-stage and the chromogenic assay when looking for possible deficiency of factor VIII.

Our patient was found to have the c.5123G>A, p. Arg1708His mutation. This is a point mutation that results in substitution of arginine by histidine at codon 1708. It has been reported previously and is associated with mild haemophilia A. Carrying out both the one-stage and chromogenic factor VIII assays, as well as the genetic mutational analysis, was crucial in this case, in order to choose a recombinant factor VIII product that allowed accurate monitoring of factor VIII levels using the

one-stage factor VIII assay as well as providing reassurance of no previously reported inhibitor development association.

As with all live donor procedures, the decision to proceed or not is made after careful consideration of the relative risks. Typically, when there is higher risk of a poor outcome after live donor kidney transplantation, this is due to the complexity of the recipient. In this instance, however, there were significant potential complications related to the donor and it was crucial that the donor himself was involved in discussion and, ultimately, the decision regarding donation to his sister. In the setting of higher risk, often the closeness of the emotional relationship between a donor and recipient is the determinant of whether a donor will proceed or not, and this was influential in this case. The patient's sister is now doing very well with excellent kidney function and the donor has no regrets regarding donation.

Learning points

- ▶ A detailed bleeding history should be taken during preoperative assessments.
- ▶ It is possible to have a bleeding disorder with a normal coagulation screen result and so a detailed bleeding history should always be taken regardless of the results of coagulation screen tests.
- ▶ A positive bleeding history along with an abnormal coagulation screen, even in the absence of known personal or family history of a bleeding disorder, should prompt referral for specialist haemostasis investigation.
- ▶ Both one-stage and chromogenic factor VIII assays should be carried out to assess factor VIII levels as either one used in isolation can underestimate the factor VIII deficiency in some cases.
- ▶ Although persons with haemophilia are not eligible to be blood donors, this case demonstrates that a person with mild haemophilia was able to be a live organ donor. This can be successfully achieved through a multidisciplinary approach.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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