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Answering reviewers

Response to reviewers:

Reviewer 1

This is good case report. However may need some inforomation #1 How long is the intestin length before and after SMA thrombosis in case 1. may need figure. #2 Describe methods and manufacture of PRA and DSA examination. #3 How was the interval and amount of PE in case 1 #4 What was direct indication for intestinal transplant in case 1 #5 How was the dose of thimogloulin and interval in case 1. PE too #6 What was recent DSA result in case 1 and 2.

- The remaining intestine was less than 5 cm of proximal jejunum and the left colon and sigmoid. The SMA territory was completely gone
- Plasmapheresis was performed prior to transplant, seven doses on alternating days followed by IVIG (10gm). Postoperatively, there was 5 doses on alternating dates.
- In case 1 the indication was short bowel syndrome due to complete SMA thrombosis after whipple procedure with arterial reconstruction.
- Thymoglobulin dose was the same as induction 100mg/kg and total of 5 doses given alternating to the plasmapheresis session every other day. Plasma exchange is every other day for a total of 5 times. No dosage.
- None of the patients had any indication of rejection during the postoperative period and surveillance DSA were not done in either of them. We acknowledge this is a limitation but our practice is to obtain DSA levels if we suspect rejection, but this was not the case in either patient.

Reviewer 2

This manuscript approaches two topics in intestinal transplantation: living donor transplants and transplantation in sensitized patients. Authors present

two cases of intestinal transplant after desensitization treatment with living donor grafts. Case #1: Recipient with strong preformed DSA, treated with multiple plasmapheresis and immunoglobulin infusions. It would be interesting to show the evolution in DSA titles during treatment. Authors do not describe the doses of neither immunosuppressive drugs nor immunoglobulin used at induction. DSA titles after transplant are not shown. PTLD is not described (type of PTLD, immunosuppression at the moment of PTLD development, location of the tumor, etc). The role of rituximab in antibodies production has not been analyzed. Case #2: Recipient with anti-HLA antibodies but no DSA, and negative cross match, so patient was not sensitized against her donor. Nonetheless the patient underwent desensitizing treatment. Living donor intestinal transplant is not integrated in all transplant programs, because it carries important ethical conflicts due to the risk of complications in donors (surgical complications, hidroelectrolitic disturbances, increased bowel movements, etc). One of the main theoretical advantages of living donor is the possibility of choosing compatible HLA donors in sensitized receptors. It seems to have no sense to perform it with a donor against the recipient has preformed antibody (Case #1). Case #2 has been treated as a sensitized recipient despite not having DSA against his donor.

Case #1: DSA were not followed after transplant, as the patient was asymptomatic. We do not routinely screen for DSA unless there is a clinical indication. This is a valid point but was not conducted in our two patients. PTLD was EBV positive biopsy proven located in multiple node above and below the diaphragm. The treatment is described. The maintenance immunosuppression was also described and we the same at the time of PTLD presentation. Rituximab was used to treat the PTLD.

Case#2: The flow cytometry crossmatch was positive for B-cell prior to transplant. No DSA were found but the PRA was very high, this cannot exclude other atypical antibodies that may cause a strong immunological reaction. The authors felt that risk of severe immune reaction was high and used the High PRA and positive XM protocol similar to the one used in kidney transplants at our institution.

Reviewer 3
The effectivity of desensitization is demonstrated by PRA and flow cytometry cross-match with channel shift. For the reliability of theses techniques the principle and the limitations should be discussed with more details.

Thank you for the comments. We will address the issue in the text provided word allowance.

Reviewer 4

This manuscript is essentially an extended case report that presents the authors' experience with transplanting cross match-positive small bowels from living donors following an intensive desensitization protocol. As the authors mention, this method/source of grafts can contribute to alleviating the shortage of acceptable donors in certain populations. To this end, the experience discussed in the manuscript is of interest. My main issue with the work is the relatively short follow-up interval (2 years and 6 months), particularly due to the numerous uncertainties related to AMR in the small bowel transplant setting. The authors make a case with their manuscript that their technique may afford short term graft survival with stringent followup including biopsies, but the interesting (and perhaps equally critical question) is what the long-term survival of these grafts will actually be. In summary, this work provides a useful starting point for larger and more regimented studies that would include longer-term follow-up. The authors should acknowledge that this represents their experience with only two patients and limited followup.

Thank you, we will add a statement.