Reviewer's report

Title: Late antibody-mediated rejection after ABO-incompatible kidney transplantation during sepsis.

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Reviewer: emanuele cozzi

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This interesting paper by de Weerd and colleagues deals with an untreatable AMR episode in a case ABOi (A into O) renal transplant coinciding with a septic event due to Serratia Marcescens. The authors speculate that the Serratia Marcescens may have triggered the production of the very high titers of anti-A antibodies observed and that these are responsible for the graft loss.

This may well be the case although evidence for an unequivocal causative link between the 2 events has not been provided.

On the other hand, it is unquestionable that:
- the titers of isoagglutinins reached in this patient are certainly compatible with AMR.
- A pyelonephritis-associated increase of the isoagglutinin IgG/IgM titers associated with a biopsy-proven AMR in a ABOi renal recipient has been reported,
- the development of infection may increases both breadth and strength of anti-HLA antibodies [reference to this paper should be added].

Still, the authors fail to provide evidence that antibodies directed to other (HLA or non-HLA) specificities may have played a causative(?)/contributory(?) role in this event.

As a consequence the reviewer strongly believes that the following points may be of help to improve the manuscript:

MAJOR COMPULSORY REVISION

1) A complete patient history (this is a female) should be provided: did she have any pregnancy? What about past transfusions?
2) The patients received transfusions perioperatively. How many blood donors were used?
3) What is the anti-HLA antibody profile prior to transplantation and at the various time points where ABO antibodies were studied? Were there any DSA at any time after transplantation (especially at the time of rejection). It would also help if anti-AT1R antibodies were studied.
4) The treatment is not comprehensible: what do the authors mean by “Rituximab 4 weeks”? Same for MMF and other drugs (including doses of IVIG). Also which
5) The reviewer disagrees with the statement: “...this patient is remarkably different....., due to the exceptionally late occurrence of AMR12 weeks after kidney transplantation ....”.. In fact, in the Tobian paper that the authors cite, 3 of the 7 episodes reported occurred 15 weeks after transplantation or later! This must be amended as needed.

6) The reviewer disagrees with the statement: “...Anti-ABO titers usually remain low after transplantation and are not boosted by the graft under adequate immune suppression”. What is the evidence behind this statement? What do you mean by “remain low”? In fact, in the Tobian paper 3 out of 8 patients WITHOUT episodes of AMR had HIGH anti-ABO antibody titers (128 or even greater).

7) The authors seem to have overlooked the fact that the titer of 1/512 in the Tobian paper refers to IgG (gamma chain!) and not IgM. So they cannot compare their >5000 data that refers to IgM (as Tobian only refers to IgG in his paper). Furthermore, the detrimental role of IgM in these patients is possibly debatable .

8) A1 and A2 donors are not equally immunogenic: Which one did you have here?

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.