IVIG-associated hemolysis[2]; therefore, only IgG was tested by DAT. As the ABO system is a carbohydrate antigen system,[7] it was not surprising that the isoagglutinins eluted from the DAT-positive patient samples were of the IgG_2 subclass.[4,6] This subclass is known to be associated with carbohydrate antigens and studies previously reported have shown that ABO isoagglutinins are primarily of the IgG_2 subclass.[4] IgG_2 subclass antibodies also are known to interact with the FcγRIIA receptor on mononuclear phagocytes,[3,6,8,9] and this interaction can be enhanced by specific polymorphisms.[8,9] Although the patients reported herein were not tested for FcγRIIA polymorphisms, we previously showed in a different cohort of patients with or without hemolysis that there is no correlation of FcγR polymorphisms with IVIG-associated hemolysis.[3]

Despite the caveat that only 10 of 22 patients' DAT-positive subclass could be determined, these results can still provide some valuable conclusions, as we were able to test 8 patients who hemolyzed and 2 patients who did not hemolyze. We conclude that in patients who develop a positive DAT following IVIG therapy the predominant antibody opsonizing the patients' autologous RBCs is an isoagglutinin of IgG_2 subclass. We further conclude that there is no correlation of IgG_2 or other subclasses to whether a patient will hemolyze or not.

CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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ABO-associated antibody-mediated rejection following A2B-to-B renal transplantation and successful treatment with therapeutic plasma exchange

Organ allocation policies allowing blood type A2(B) donor to B recipient renal transplantation came into effect in December 2014 as an effort to increase allograft access for blood type B transplant candidates. For B candidates to be listed to receive A2(B) donor kidneys, a pretransplantation anti-A IgG titer using A2 cells (A2-IgG) must be 4 or less ("low"). Long-term follow-up has demonstrated that A2(B)-to-B transplants with previously low A2-IgG titers have noninferior clinical outcomes when compared to B-to-B transplants.[1,2]

We report a case of a 64-year old B-positive male with end-stage renal disease secondary to type 2 diabetes mellitus, cirrhosis, and hypertension, who had been actively listed for a renal transplant for 2 years. At the time of his transplant from an A2B donor, his panel reactive antibodies demonstrated 0% reactivity for both HLA class I and class II antigens, and his A2-IgG was 1:1 or 1:2 by doubling dilution tube method using the patient's serum and A2 cells on four occasions; the closest testing was 52 days before the transplant. Per institutional protocol, his immunosuppression regimen consisted of

doi:10.1111/trf.15201

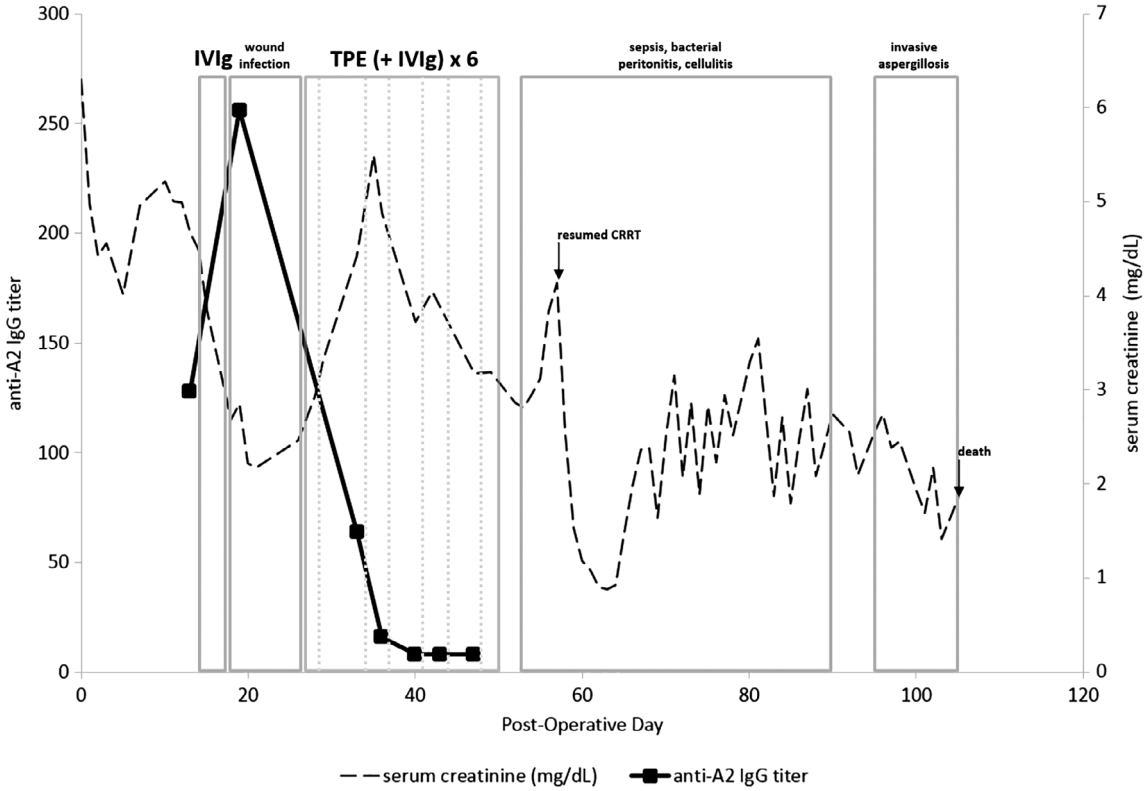

Fig. 1. Anti-A2 IgG titer and serum creatinine over patient post-operative clinical course.

thymoglobulin, tacrolimus, mycophenolate mofetil, and prednisone. His posttransplant course was complicated by slow serum creatinine decrease in the context of supratherapeutic tacrolimus levels. He was discharged on Postoperative Day 4 with a creatinine of 4.56 mg/dL.

The patient was readmitted on Postoperative Day 10 for increased incisional drainage, leukocytosis, and rising creatinine. Imaging revealed a fluid collection around his allograft that required surgical exploration and wound washout of his fascial dehiscence. Culture of his abdominal fluid grew *Streptococcus viridans* and coagulase-negative *Staphylococcus.* At the time of wound washout on the next day of transplant, an allograft biopsy was obtained that revealed diffuse peritubular capillary C4d staining with occasional neutrophils suggestive of acute antibody-mediated rejection; no evidence of T-cell–mediated rejection was observed. Repeat HLA panel reactive antibodies was negative, but his A2-IgG titer was elevated to 128 (Fig. 1). Repeat testing 1 week later showed an A2-IgG titer of 256; however, this was after administration of IVIG (2 g/kg), which also contains ABO antibodies that have been variably associated with hemolysis.[3,4] Antimicrobial therapy for his wound infection precluded additional immunosuppressive therapy for rejection for another week. He then began a course of six treatments of one plasma volume therapeutic plasma exchange followed by IVIG administration (100 mg/kg) roughly every other day per institutional protocol for renal antibody-mediated rejection. During and following this course, his A2-IgG titers declined steadily to 1:8 after 3 therapeutic plasma exchange procedures and his creatinine also gradually reduced (Fig. 1). Unfortunately, the patient continued to have infectious events and died at Postoperative Day 105 after developing disseminated invasive aspergillosis.

Breimer et al.[5] demonstrated weak A antigen expression on human renal endothelium and distal tubules in A2 individuals by immunohistochemistry. To our knowledge, proven ABO-mediated antibody-mediated rejection has not been reported in an A2(B) transplant to a B recipient. There is strong circumstantial evidence supporting stimulation of A2-IgG titer by the transplanted graft, especially in this patient with serial negative A2-IgG titers before transplant. We also think the rise in isohemagglutinin was likely enhanced by infection. We highlight this case to demonstrate the possibility of developing A2-IgG following transplant of an A2 kidney to a non-A recipient, as well as to offer an anecdote of effective treatment with therapeutic plasma exchange followed by IVIG that subsequently decreased antibody titers and creatinine.

CONFLICT OF INTEREST

A.S.T. has disclosed no conflict of interest. L.C. and C.Y. are members of AABB committees.

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