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# Anti-A Production by a Group 0 Spleen Transplanted to a Group A Recipient

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**Abstract.** A group $A_1$ diabetic received a pancreas-spleen transplant from a group 0 donor. Severe immune hemolysis due to anti-A ensued, requiring graft splenectomy. The transplanted spleen can be a potent source of blood group antibody.

## Introduction

The temporary appearance of anti-A or anti-B isohemagglutinins in non-group 0 patients receiving a transplanted organ from a group 0 donor has been observed following transplantation of lung [1], kidney [2–4], and liver [5]. We have investigated a case of anti-A formation and severe hemolysis following pancreas-spleen transplantation from a group 0 donor into a group A recipient.

## Materials and Methods

The patient's serum was tested for the presence of ABO antibody activity at room temperature (RT), 37 °C, and by antiglobulin testing with freshly drawn $A_1$, $A_2$, B, and 0 red blood cells (RBC). The direct antiglobulin tests, 56 °C heat eluates, and dithiothreitol (DTT) treatment of the serum were performed by established procedures [6]. Agglutination reactions were scored as described by *Issitt and Issitt* [7].

## Case History and Results

The patient was a group $A_1$ 35-year-old white male admitted for pancreas transplantation. He had been a diabetic requiring insulin injections since the age of 5. In addition to neuropathy and retinopathy, in 1981 he developed renal failure and required dialysis. In December 1982 he received a successful cadaveric kidney transplant with cyclosporine immunosuppression. Despite a strict insulin regimen, his blood glucose ranged between 44 and 425 mg/dl, without good control. On March 6, 1983, he received a cadaveric pancreas transplant from a group 0 donor. The donor pancreas, spleen, and a segment of duodenum were transplanted en bloc, with the duodenum anastomosed to the recipient's jejunum [8]. The recipient's pancreas and spleen were left in situ. The estimated blood loss during surgery was about 100 ml. No blood products were

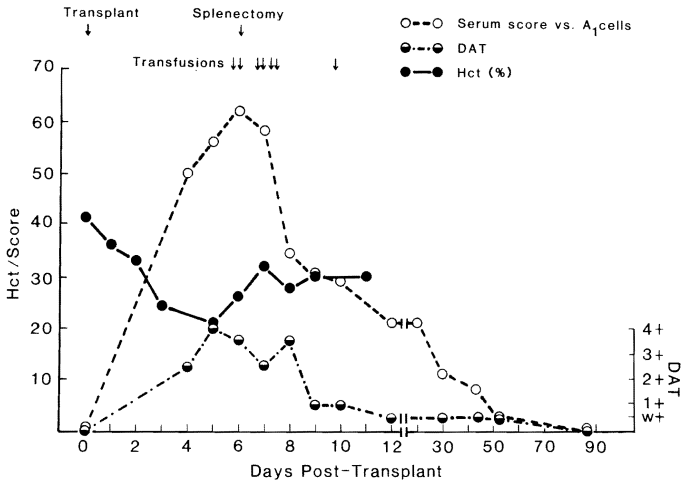


**Fig. 1.** Serologic and hematologic course after transplantation of group 0 spleen to group $A_1$ recipient.

transfused. A course of corticosteroids was added to the ongoing cyclosporine immunosuppression.

The patient's clinical course is illustrated in figure 1. The hemoglobin and hematocrit on the day of surgery were 13.8 g/dl and 41.3%, but fell steadily over the first 5 postoperative days to 7.4 g/dl and 21%, respectively, with no evidence of hemorrhage. At this time, the haptoglobin was 35 mg/dl and reticulocyte count 5.5%. Direct and indirect serum bilirubin were 1.0 and 2.9 mg/dl, respectively. The urine was positive for urobilinogen. The platelet count declined from a preoperative level of $232 \times 10^9$/l to $137 \times 10^9$/l by the 7th postoperative day.

Prior to surgery, the direct and indirect antiglobulin tests were negative. Because of the falling hematocrit, blood was ordered crossmatched for transfusion 4 days after surgery. Group A units were found to be incompatible at RT (1+), 37 °C (1+) and by antiglobulin testing (3+). The direct antiglobulin test (DAT) was positive (broad spectrum 4+, anti-IgG 3+, anticomplement 1+). Antibody eluted from the patient's RBC agglutinated $A_1$ cells (4+) and $A_2$ cells (1+), but not group 0 cells. From days 4–6 postoperatively, serum anti-A agglutination scores against group $A_1$ cells at RT, 37 °C, and at the antiglobulin phase, rose from 10, 5, and 50 to 10, 10, and 62, respectively. DTT treatment of the patient's serum reduced the scores only slightly. No reactivity was observed when testing the patient's serum against $A_2$ cells. After absorption of the serum with $A_1$ cells, an eluate from these cells reacted 1+ with $A_1$ cells, very weakly with $A_2$ and B cells, and was negative with group 0 cells. On day 6, the transplanted spleen was removed. The spleen weighed 190 g (normal 150 g); histopathology showed prominent immunoblastic proliferation and red pulp congestion, consistent with immune stimulation and hemolysis. During and after splenectomy the patient received a total of 7 units of washed group 0 RBC.

After splenectomy the anti-A scores fell steadily but the antibody was still detectable 7.5 weeks later. The patient's hematocrit

stabilized and his blood glucose became normal. All evidence of anti-A disappeared by 3 months, and was also absent 1 year later.

## Discussion

This group $A_1$ patient had severe immune hemolysis due to anti-A after transplantation of a group 0 spleen with a pancreatic graft. The antibody was of $A_1$ specificity, though a trace of anti-AB activity was detectable in the serum. While it is likely that plasma containing anti-A was administered passively along with the transplanted organs, the following evidence indicates that the transplanted spleen was actively producing anti-A isohemagglutinins: (1) The volume of plasma in the transplant was undoubtedly small and would be diluted substantially in the recipient's plasma. (2) Plasma anti-A levels rose significantly between postoperative days 4 and 6, indicating synthesis of new antibody. (3) The DAT also increased in strength during this period of time. (4) Splenectomy of the graft reversed this process. (5) The spleen showed evidence of immune stimulation on histological examination. We conclude that the spleen, a large lymphoid organ, produced a marked graft-versus-host anti-A isohemagglutinin response when challenged by the transplant recipient's $A_1$ antigen.

Inclusion of the spleen in total pancreatic transplantation offers several possible advantages [8]. The splenic vessels supply much of the pancreatic venous drainage, and preserving them in toto may help prevent splenic vein thrombosis, a common problem in this procedure. Intraoperative trauma to the pancreas may be lessened by a wider en bloc dissection. Experimental evidence suggests a protective effect of splenic transplantation on survival of other concomitant organ grafts, including the pancreas [9]. However, as shown in our case, the donor should have the same ABO group as the recipient, an important consideration in future transplants of this kind.

A case similar to ours was reported in 1964 [10]. In an experimental protocol attempting transfer of tumor immunity to patients with carcinoma, 1 group A recipient received a group 0 spleen. Severe hemolysis ensued. While being prepared for splenectomy, the patient aspirated and died. The pathogenesis of this hemolysis was undoubtedly the same as in our case.

Anti-recipient ABO antibody has occasionally been reported after other instances where a group 0 organ was transplanted to a group A recipient. *Beck* et al. [1] noted a lung transplant patient in which a positive direct antiglobulin test occurred. 3 0-to-A kidney transplants have been followed by mild to moderate hemolysis due to anti-A, the antibody persisting for up to 60 days after surgery [2–4]. We have studied 8 cases of moderate to severe hemolysis due to anti-recipient ABO antibody after unmatched liver transplantation, including recipients who were group B and AB as well as group A [5]. In addition to the spleen, the largest lymphoid organ, these other grafts apparently also can contain enough lymphocytes to form clinically significant antibodies to host red cells, even in the setting of posttransplant immunosuppression.

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## Addendum

Since this manuscript was submitted, two additional reports have appeared of ABO antibodies attributable to unmatched renal transplants [1, 2].


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