

Treatment of Pure Red-Cell Aplasia With Cyclosporine in a Renal Transplant Patient

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Abstract

Acquired pure red-cell aplasia is a rare disorder that can be either idiopathic or associated with certain autoimmune diseases, pregnancy, lymphoproliferative disorders, nutritional deficiencies, or medicines. We present a deceased-donor renal transplant patient who developed pure red-cell aplasia associated with mycophenolate mofetil or tacrolimus and was treated with cyclosporine. A 20-year-old woman was transplanted from a deceased donor 1 month earlier and presented to us with symptoms of fatigue, prostration, and palpitation. The results of a laboratory examination revealed anemia. A diagnostic work-up resulted in a diagnosis of pure red-cell aplasia. Mycophenolate mofetil was discontinued. Tacrolimus also was replaced with cyclosporine 2 months after mycophenolate mofetil was halted because of a lack of improvement in anemia. Three months later, her anemia improved with cyclosporine. Starting cyclosporine instead of tacrolimus or mycophenolate mofetil showed good improvement in our patient within 6 months of therapy.

Key words: Renal transplantation, Pure red-cell aplasia, Cyclosporine A

Introduction

Acquired pure red-cell aplasia (PRCA) is a rare disorder and can be either idiopathic or associated

with certain autoimmune diseases, pregnancy, lymphoproliferative disorders, nutritional deficiencies, or medications. In rare cases, it has been reported to coexist with other autoimmune cytopenias.¹ There have been reports of PRCA after immune suppression with tacrolimus and mycophenolate mofetil in transplanted patients.²⁻⁴ We present a deceased-donor renal transplant patient who developed PRCA, which was caused by either mycophenolate mofetil or tacrolimus and treated with cyclosporine.

Case Report

The patient is a 20-year-old woman who had been in renal replacement therapy for 6 years. She had received a transplant from deceased donor 1 month earlier. She presented to our outpatient clinic with a 2-week history of fatigue, prostration, and palpitation that had become more severe over the previous week. She had already been taking mycophenolate mofetil 1 g/d, tacrolimus 7 mg/d, and corticosteroids 17.5 mg/d. The results of a physical examination were paleness of the skin and conjunctivae, and a 2/6 systolic heart murmur that could be heard on all auscultation sites of the heart. Laboratory findings were hemoglobin 46 g/L, leukocyte count $7.5 \times 10^9/L$, platelet count $429 \times 10^9/L$, reticulocyte 0.1 %, mean corpuscular volume 95 fL, red cell distribution width 19%, lactate dehydrogenase 259 IU/L (range, 150-450 IU/L). The results of direct and indirect Coombs' tests were negative, serum creatinine was 1.2 mg/dL. The results of an enzyme-linked immunosorbent assay for viral infections (ie, hepatitis B, C, D, cytomegalovirus, Epstein-Barr virus, parvovirus B19, and toxoplasma, other viruses, rubella, and herpesvirus [TORCH]) were negative. Results of

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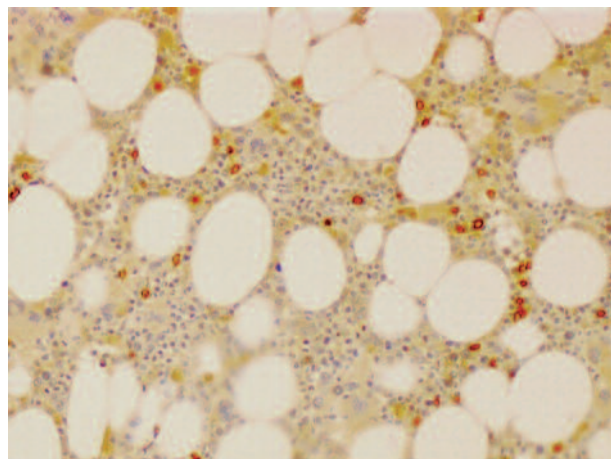
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biochemical evaluation for vitamin B12 and iron deficiency were normal. The results of a bone marrow examination showed a prominent decrease in the erythroid series (Figure 1). Mycophenolate mofetil was discontinued. Immunohistochemical investigation of bone marrow for viral infection (eg, parvovirus B19) was not done because we lacked laboratory techniques. Tacrolimus also was replaced with cyclosporine 2 months after mycophenolate mofetil was stopped owing to a lack of improvement in anemia. Three months after beginning cyclosporine therapy, her hemoglobin was 118 g/L; six months later it was 134 g/L. Her serum creatinine was 70.7 $\mu\text{mol/L}$, and she had proteinuria 100 mg/d one year after transplant.

Figure 1. Bone Marrow Trephine Biopsy Specimen Showing Prominent Decrease in Erythroid Series; Stained With Glycophorin A



Discussion

Pure red cell aplasia is an autoimmune disorder characterized clinically by a selective decrease in erythrocytes and their progenitors in the peripheral blood and bone marrow.⁵ The patient developed severe anemia after renal transplant with selective absence of erythroid cells in the bone marrow, leading to a diagnosis of PRCA. A response to autoimmune PRCA has been obtained with various immunosuppressive regimens including corticosteroids, cyclosporine, azathioprine, alkylation agents, or anti-thymocyte globulin, tacrolimus, and intravenous immunoglobulin.^{1,3,5}

Mycophenolate mofetil is used in immune suppressive therapy in adult or childhood allogenic

renal, cardiac, or hepatic transplant patients in combination with corticosteroids and cyclosporine.⁶ Pure red cell aplasia related to mycophenolate mofetil therapy has been reported in 41 cases with 18 of them achieving normal hemoglobin levels with either cessation or escalation of mycophenolate mofetil dosage.⁷ It has been reported that PRCA in transplant patients is associated with mycophenolate mofetil and combined use of other immunosuppressive agents including alemtuzumab or daclizumab.² Our patient was not treated with any of these agents. Emergence of mycophenolate mofetil-related PRCA has been seen in the early posttransplant period and also, hematologic improvement has been seen immediately after ceasing mycophenolate mofetil in some case reports and in solid-organ transplant series.^{2,3}

In our case, although severe anemia occurred immediately postoperatively, cessation of mycophenolate mofetil did not result in recovery of the patient. The effectiveness of cyclosporine in treating PRCA is 65% to 87%. Of note is that a high dosage was used to obtain these results (12 mg/kg/d). That accompanies with adverse effects and relapses are not uncommon. Also there are case reports of PRCA (either idiopathic or secondary) treated successfully with cyclosporine.⁸ Besides, tacrolimus is another immunosuppressive agent commonly use, and PRCA cases related with tacrolimus have been reported.⁹ In comparison, tacrolimus is an agent that has been shown to be an alternative treatment option for PRCA in patients who fail to respond to cyclosporine.¹⁰

In conclusion, while immunosuppressives have been used to treat PRCA, there are reports of transplant-related PRCA caused by these immunosuppressive agents (eg, mycophenolate mofetil, tacrolimus, intravenous immunoglobulin, and cyclosporine). This may be overcome by alternating immunosuppressives as we did. It should be borne in mind that cyclosporine, as with any immunosuppressive agent, may yield recovery as early as 6 months in PRCA, even when recovery is not achieved, despite discontinuing mycophenolate mofetil and tacrolimus.

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