



Hemolytic Anemia as Presentation of T-Cell Large Granular Lymphocytic Leukemia After Kidney Transplantation: A Case Report

Gaetano Alfano^{a,b,*}, Annachiara Ferrari^a, Francesco Fontana^b, Francesca Damiano^b, Andrea Solazzo^a, Giacomo Mori^b, and Gianni Cappelli^{a,b}

^aSurgical, Medical and Dental Department of Morphologic Sciences, Section of Nephrology, University of Modena and Reggio Emilia, Modena, Italy; and ^bNephrology Dialysis and Transplant Unit, University Hospital of Modena, Modena, Italy

ABSTRACT

T-cell large granular lymphocytic (T-LGL) leukemia is a rare clonal proliferation presenting with cytopenia, splenomegaly, and autoimmune manifestations. It has rarely been described in recipients of solid organ transplants.

We report the clinical case of a young kidney transplant recipient that developed T-LGL leukemia 3 years after kidney transplantation. The disorder manifested with a severe form of autoimmune hemolytic anemia in the absence of other laboratory abnormalities. The anemia was successfully treated with an intense course of corticosteroids and withdrawal of immunosuppressive therapy from a calcineurin inhibitor to sirolimus, a mammalian target of rapamycin inhibitor.

Our case shows that autoimmune hemolytic anemia can be a life-threatening manifestation of T-LGL disease. The antiproliferative effects of sirolimus may be useful in the treatment of symptoms of T-LGL leukemia in kidney transplantation.

T-CELL large granular lymphocytic (T-LGL) leukemia is a clonal proliferation of large granular lymphocytes. Cytopenia, splenomegaly, and autoimmune phenomena are the main manifestations of this lymphoproliferative disease [1–3]. T-LGL leukemia has been rarely described in recipients of solid organ transplants [4,5]. Prognosis of the disease is generally favorable since progression to the malignant variant is rarely reported in the general population [6]. Treatment is based on immunosuppressive therapy including cyclosporin, cyclophosphamide, and methotrexate, but there is a lack of specific guidelines [7]. We report a case of T-LGL leukemia in a young recipient of a kidney transplant (KT) manifesting with hemolytic autoimmune anemia. Treatment with corticosteroids and a therapeutic switch from tacrolimus to sirolimus resolved the severe episode of anemia and ensured good graft function.

CASE PRESENTATION

A 21-year-old Caucasian man with a second kidney transplant presented at our office for progressive weakness and dizziness. He had a diagnosis of end-stage renal disease due to congenital renal dysplasia at the age of 8 years. After 1 year of peritoneal dialysis, he received cadaveric kidney transplantation that failed as a result of chronic humoral rejection after 9 years.

At the age of 19 years, after 1 year of hemodialysis, a second kidney transplant from a cadaveric donor was performed. Induction immunosuppressive therapy consisted of antithymocyte globulin and high doses of corticosteroids. A maintenance immunosuppressive regimen was based on tacrolimus, corticosteroids, and mycophenolic acid. The post-transplantation course was uneventful, and the patient was discharged with normal renal function. A diagnosis of asymptomatic T-LGL leukemia was performed after the detection of relative lymphocytosis noted on the complete blood count. Bone marrow biopsy confirmed the presence of clonal LGLs of T-cell lineage in the marrow. Diagnostic work-up showed mild splenomegaly (longitudinal diameter of 13 cm) and the absence of autoimmune phenomena.

Three years after transplantation, the patient was admitted to hospital with severe anemia (7 g/dL) without other complete blood count abnormalities. He was afebrile and with normal blood pressure on clinical examination. In absence of evident bleeding, he denied melena, hematemesis, or epistaxis. A diagnosis of autoimmune hemolytic anemia associated with T-LGL leukemia was made after the

*Address correspondence to Gaetano Alfano, Nephrology Dialysis and Transplant Unit, University Hospital of Modena, Via del Pozzo, 71, 41124 Modena, Italy. E-mail: gaetano.alfano@unimore.it

detection of warm antibodies (IgA and IgG) on Coombs test. High direct bilirubin, high lactate dehydrogenase, and low haptoglobin concentration supported the diagnosis of intravascular destruction of red blood cells.

The anemia was treated with blood transfusions and corticosteroids at a dosage of 100 mg daily for 10 days, then tapered to 1 mg/kg for 5 weeks. In order to control the lymphoproliferative disorder, immunosuppressive therapy was switched from tacrolimus to sirolimus, a mammalian target of rapamycin inhibitor with well-known antiproliferative properties.

Forty-two months after successful treatment of hemolytic autoimmune anemia, serum hemoglobin level was stable to 13 g/dL and renal function was normal (serum creatinine 1 mg/dL). The rise of the mean fluorescence intensity of a pre-existing donor-specific antibody prompted the prudential conversion from sirolimus to tacrolimus after 35 months from the therapeutic switch. Despite sirolimus withdrawal, T-LGL leukemia did not progress to a malignant variant and LGL count was stable at 1000 cells/mm³.

DISCUSSION

We presented to the best of our knowledge the first case of hemolytic autoimmune anemia resulting from T-LGL leukemia in a recipient of KT. T-LGL leukemia is a rare and indolent lymphoproliferative disease which occurs with cytopenia and autoimmune phenomena. Anemia is present in about half of patients, and 20% of them require blood transfusions. T-LGL leukemia is considered to be an indolent disorder by the hematologic community and is treated with immunosuppressive therapy. In our case, we described the late and severe manifestations of T-LGL leukemia in a young recipient of KT. Although anemia was easily treated with corticosteroids, this hematologic disease threatened patient life and graft survival. Namely, the transfusions of multiple packed red blood cell units exposed the patient to different antigens that could have increased the risk of allograft rejection. The use of additional immunosuppressive agents further reduced the immune competence of an already immunocompromised patient. In addition, administration of

high-dose corticosteroids may have increased the risk of metabolic and vascular complications in our patient. The use of sirolimus is an attractive option for patients with a post-transplant lymphoproliferative disorder (PTLD) [8]. However, the minor immunosuppressive potency of sirolimus compared to a calcineurin inhibitor should be balanced against its well-known antiproliferative activity [9]. In light of these findings, we suggest a careful follow-up in all patients with T-LGL leukemia for the risk of late and sudden development of severe manifestations. Furthermore, if the patient is treated with sirolimus, it is advisable to regularly check renal function, urine examination, and de novo donor-specific antibody formation.

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