T-Cell Large Granular Lymphocytes Leukemia (T-LGL) In Kidney Transplant and Review of the Literature

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Introduction

T-cell large granular lymphocytes leukemia (T-LGL) is a rare clonal proliferation of cytotoxic lymphocytes. Diagnosis of T-LGL leukemia is based on identification of LGL lymphocytosis by peripheral blood flow cytometry. T-LGL leukemia has been defined in the World Health Organization classification of lymphoid neoplasms as a persistent (> 3-6 months) increase in LGLs count (> 2 x 10^9/L) without a clearly identified cause[1]; it was later recognized that also a lower count (i.e. < 2 x 10^9/L but > 0.4 x 10^9/L) may be compatible with the diagnosis.[2] Assessment of clonal rearrangement of T-cell receptor by PCR or Southern blotting has been considered mandatory to differentiate T-LGL leukemia from reactive polyclonal expansion. Generally**, the disease has an indolent clinical course in one third of patients**. Clinical presentation is dominated by **anemia, thrombocytopenia, neutropenia, splenomegaly, autoimmune phenomena, and tissue invasion of marrow, spleen and liver**[2]. **There are few data describing this disorder in solid organ transplant (SOT) recipients**. We determined clinical behavior of T-LGL in a population of KT recipients, and conducted a systematic review of literature recording all cases of T- LGL in SOT.

Methods

We reviewed the charts of 629 kidney transplants recipients in follow-up care from January 1998 to April 2016. T-LGL cases have been detected by peripheral blood flow cytometry which was performed for clinical indications. In addition, we researched, through PubMed, English-language reports of T-LGL in SOT from March 1981 to September 2016. The search keywords or text words on were “large granular lymphocyte leukemia”, “T-cell large granular lymphocyte leukemia”, “aggressive T-cell large granular lymphocyte leukemia” and “organ transplantation”.

Results

We found 6 cases of T-LGL leukemia in our KT recipients and reviewed 10 cases[3-6] from literature . Main characteristics of the cases are summarized in table 1 .T-LGL leukemia was detected in 14 kidney, 1 liver and 1 combined liver-kidney transplant recipients. Average age was 48.2 years (range 20-69 years) with a male predominance (62.5%). The disease developed after a means age of 9.5±5.6 years from transplantation. **Anemia was the most common presentation** (68.7%) followed by lymphocytosis (50%), thrombocytopenia (18.7%) and neutropenia (6%). Splenomegaly was reported in 37.5% of our patients. **Eight patients (50%) underwent antineoplastic treatment for the severity of clinical manifestations**. After a mean follow-up of 3 years, 5 subjects (62.5%) had a good outcome whereas **3 (37.5%) remained red blood cell transfusion-dependent. No cases progressed to aggressive T-LGL leukemia or died of cancer.**

Table 1. Clinical and laboratory characteristics of patients with T-LGL

Number of cases	**16**
Graft: kidney / liver / combined kidney-liver	**14 / 1 / 1**
Male: Female ratio	**1.66:1**
Mean age at diagnosis (years)	**48,2±13,8**
Interval transplant-diagnosis (years)	**9.5**
Immunosuppressive therapy CyA / FK / mTORi / CnI+mTORi	**8 / 5 / 2 / 1**
Mean lymphocyte / T-LGL counts at presentation (cells 10^9/l)	**5.99 / 1.7**
TCR αβ / γδ / NA	**44.4% / 16.7% / 38.9%**
Hematological complication	
hemolytic anemia	**25% (4/16)**
PRCA	**12.5% (2/16)**
anemia NOS	**31.25% (5/16)**
Lymphocytosis	**50% (8/16)**
Autoimmune thrombocytopenia	**6.25% (1/16)**
Splenomegaly	**60% (6/10)**
Blood transfusion	**56.25% (9/16)**
Specific chemotherapy	**50% (8/16)**
Splenectomy	**12.5% (2/16)**
Transfusion dependent at the end of follow-up	**18.75% (3/16)**
Mean follow-up (months)	**35.9**
Survival at the end of follow-up	**100% (16/16)**
Graft function at the end of follow-up	
graft loss	**18.75% (3/16)**
stable graft function	**50% (8/16)**
NA	**31.25% (5/16)**

TCR, T-cell receptor; EBV, Epstein Barr Virus; CMV, Cytomegalovirus; PRCA, pure red cell aplasia; SOT, solid organ transplant; CnI, Calcineurin inhibitors; mTORi, mammalian target of Rapamycin inhibitors; NA, non aviable.

Conclusion

T-LGL is a rare but potentially disruptive hematological disorder in SOT recipients. The main clinical manifestation is anemia, often red blood cell transfusion-dependent. Its association with clinical symptoms and its potential for requiring specific chemotherapy suggests that T-LGL should be considered as part of the spectrum of post-transplant lymphoproliferative disorders of T-cell lineage. Further reports of T-LGL in SOT are mandatory to understand its clinical course and best treatment.

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