Abstract

Post-transplant lymphoproliferative disorders (PTLDs) are life-threatening complications of solid-organ transplantation and bone marrow transplantation leading to a high mortality. PTLD represents a heterogeneous group of lymphoproliferative diseases. They become clinically relevant because of the expansion of transplantation medicine together with the development of potent immunosuppressive drugs associated now with long survival. The risk of PTLD is highest in the early post-transplant period, but the cumulative risk increases with time. We report a case of two sequential malignancies – carcinoma bladder occurring -13 years and now gastric lymphoma -15 after renal transplantation in a 73-year-old man.

Introduction

The term ‘post-transplant lymphoproliferative disorder’ or disease (PTLD) was first introduced in 1984 by Starzl. Today, it represents a heterogeneous group of lymphoproliferative diseases, ranging from Epstein–Barr virus (EBV)-associated polyclonal proliferation to highly aggressive monomorphic proliferations, such as diffuse large B-cell lymphoma (DLBCL). The reported incidence of PTLD is very variable as is its related mortality (30–60%). The clinical picture, intensity of immuno-suppression, primary and co-existing diseases and PTLD location are also quite variable.

Case Report

A 73-year-old male on immunosuppressive therapy was admitted to hospital with long standing gaseous dyspepsia and pain abdomen. Earlier, he had recurrent pyelonephritis which had caused end-stage renal disease in this patient, who received a cadaveric renal graft in Jan 1999. His induction immunosuppression had been on azathioprine, and prednisone. A induction immunosuppression had been maintained on azathioprine, and prednisone. A necrotic ulcer in the greater curvature. An endoscopic biopsy confirmed high grade NHL (DLBCL type). On IHC LCA & CD20 was positive with AE1/AE3 negative. The lymphomatous gastric ulcer was also involved with candida. Bone marrow aspirate & biopsy revealed 40% cellularity & excluded lymphomatous involvement in bone marrow. He was staged to Stage IIA extra-nodal NHL and was treated with R-CHOP (renal chemotherapy with continuation of immuno-suppression and antifungal therapy with IV Anidulafungin.

Discussion

Lymphoproliferative malignancies occur in about 10% of patients after solid organ transplantation. In renal allograft recipients, the incidence of PTLD is about 1%. Of PTLD cases, T-cell lymphoma accounts for about 10% – 15%. The incidence of PTLD cited in studies varies because of a lack of standardized inclusion criteria. In a multicenter analysis of more than 50,000 kidney and heart transplant recipients from North America and Europe, the incidence of non-Hodgkin lymphoma (NHL) was higher during the first year after transplantation; it declined in subsequent years.

Heart–lung recipients showed the highest relative risk (at 239.5) among the various types of solid organ transplants. The Collaborative Transplant Study database was used to evaluate graft survival and NHL at 3 years according to type of induction therapy in 112,122 patients receiving a deceased-donor renal graft during 1985 – 2004. Graft survival was significantly improved with induction using thymoglobulin and interleukin-2 receptor antibody, but an increased risk of lymphoma was associated with induction therapy using muromonab-CD3 or antithymocyte globulin.

Recently, Kirk et al. analyzed the data on approximately 60,000 kidney recipients from the Organ Procurement and Transplantation Network/United Network for Organ Sharing database, looking for a relationship between induction agent and PTLD. Thymoglobulin was associated with a significantly increased risk for PTLD (p = 0.0025), but alemtuzumab (p = 0.74), basiliximab (p = 0.33), and daclizumab trended toward a protective effect (p = 0.06). Patients receiving chronic treatment with prednisone and azathioprine are at increased risk for developing NHL. Randomized trials did not find any difference in the risk of PTLD development with the use of cyclosporine and tacrolimus. Some, but not all, registries suggest that risk increases by a factor of 1.5 – 2 with the use of tacrolimus compared with cyclosporine. Infection with EBV is an important causative factor in the origin of most B-cell PTLDs. Although several cases of T-cell lymphoma has been described in EBV-positive patients, the associations are not very well established. Opelz et al. analyzed the Collaborative Transplant Study database for known pre-transplant EBV and cytomegalovirus serostatus and occurrence of NHL. Regardless of age,
negative EBV serostatus pre-transplant was significantly associated with risk of NHL in kidney transplant recipients (p < 0.001). The risk of PTLD in EBV-negative recipients was increased by a factor of 6. Cytomegalovirus serostatus was not independently associated with risk of NHL after kidney transplantation. Most T-cell lymphomas occur several years post transplantation; very few cases of T-cell PTLD have been reported during the first year post transplantation. Our patient developed T-cell lymphoma 17 years after receiving her renal graft. Only 1 case of T-cell lymphoma occurring that late after renal transplantation has previously been reported. The outcome of PTLD is usually poor. Based on the Collaborative Transplant Study database, the 1-year mortality was 40% – 50%, which has not improved. The poor prognostic factors include late onset, older recipient age, high lactate dehydrogenase, poor performance status, T-cell PTLD, and multi-system disease. Treatment for PTLD is still equivocal. Reduction of immunosuppression is helpful in early disease. Surgical removal and radiation therapy are useful for localized lesions. Cytotoxic and antiviral drugs have been reported to be helpful in selected cases. In our patient, poor prognosis prompted the family to opt for comfort care; no treatment was attempted.

References