Post-transplant lymphoproliferative disease (PTLD) is a rare but life-threatening complication after solid organ transplantation. The risk of PTLD varies with recipient age, serostatus of the donor and the recipient for Epstein–Barr virus, type of organ transplanted, and intensity of immunosuppression. The risk of PTLD is highest in the early post-transplant period, but the cumulative risk increases with time. We report a case of PTLD occurring 17 years after renal transplantation in a 59-year-old woman.

Key words
Kidney transplant, lymphoma, T cell

Introduction
Post-transplant lymphoproliferative disease (PTLD) is a well-known complication of renal transplantation. Most cases occur in the early post-transplant period, typically during the first year after transplantation. More than 80% of post-transplant lymphomas are of B-cell origin; approximately 15% are T-cell lymphomas. Few cases of T-cell lymphoma after renal transplantation have been reported. We present a case of late-onset T-cell PTLD that occurred 17 years after the original transplantation in a patient with a renal graft.

Case report
A 59-year-old white woman on peritoneal dialysis (PD) was admitted to hospital with fever, chills, diarrhea, and fatigue.

Earlier, recurrent pyelonephritis had caused end-stage renal disease in this patient, who received a cadaveric renal graft in 1994. Her induction immunosuppression had been antithymocyte serum, and she had been maintained on azathioprine, cyclosporine, and prednisone. A transplant-kidney biopsy in 2003 for worsening creatinine showed only 10% interstitial fibrosis without acute rejection. Her graft failed in July 2009, and in December 2009, she was started on PD, which had been going well. She was also being maintained on low-dose immunosuppression because of residual renal function from the transplanted kidney.

Laboratory data on admission showed new anemia, thrombocytopenia, and leukocytosis with high lactate dehydrogenase. Cultures of blood, urine, and effluent were sterile. Abdominal computed tomography imaging showed thickening of the gastric mucosa. Upper gastrointestinal endoscopy and colonoscopy did not reveal malignancy. Titers for cytomegalovirus, BK virus, and Epstein–Barr virus (EBV) were undetectable by polymerase chain reaction. Transfusion-dependent thrombocytopenia and lymphocytosis with neutropenia led to bone-marrow biopsy, which showed T-cell lymphoma. Owing to poor prognosis, the patient was given comfort care, and she died 2 days after the diagnosis.

Discussion
Lymphoproliferative malignancies occur in about 10% of patients after solid organ transplantation (1). In renal allograft recipients, the incidence of PTLD is about 1%. Of PTLD cases, T-cell lymphoma accounts for about 10%–15% (2). 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. During the first year, the NHL incidence was higher in North America than in Europe (relative risk: 2.12; 95% confidence interval: 1.55 to 2.89) (3). Over a 10-year period, the risk of PTLD in renal recipients was 11.8 times that in a matched non-transplanted population ($p < 0.0001$). Heart–lung recipients showed the highest relative risk (at 239.5) among the various types of solid organ transplants (4).

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 (5).

Recently, Kirk et al. (6) 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 (4).

Infection with EBV is an important causative factor in the origin of most B-cell PTLDs (7). Although several cases of T-cell lymphoma have been described in EBV-positive patients, the associations are not very well established. Opelz et al. (8) 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 (9). 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 (10).

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 (11,12).

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.

Conclusions
Late-onset post-transplant T-cell lymphomas remain a rare complication of renal transplantation. The exact cause remains unclear, but aggressive immunosuppression might play an important role. These conditions have a poor prognosis, and most patients die within days or months of diagnosis.

Disclosures
The authors have no financial conflicts of interest to declare.

References

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