Posttransplant Lymphoproliferative Disorder Following Kidney Transplantation: A Review

Ben Sprangers, Leonardo V. Riella, and Daan Dierickx

Posttransplant lymphoproliferative disorder (PTLD) is one of the most feared complications following kidney transplantation. Over a 10-year period, the risk of PTLD in kidney transplant recipients (KTRs) is 12-fold higher than in a matched nontransplanted population. Given the number of kidney transplants performed, KTRs who experience PTLD outnumber other organ transplant recipients who experience PTLD. Epstein-Barr virus infection is one of the most important risk factors for PTLD, even though 40% of PTLD cases in contemporary series are not Epstein-Barr virus–associated. The overall level of immunosuppression seems to be the most important driver of the increased occurrence of PTLD in solid organ transplant recipients. Reduction in immunosuppression is commonly accepted to prevent and treat PTLD. Although the cornerstone of PTLD treatment had been chemotherapy (typically cyclophosphamide-doxorubicin-vincristine-prednisone), the availability of rituximab has changed the treatment landscape in the past 2 decades. The outcome of PTLD in KTRs has clearly improved as a result of the introduction of more uniform treatment protocols, improved supportive care, and increased awareness and use of positron emission tomography combined with computed tomography in staging and response monitoring. In this review, we will focus on the most recent data on epidemiology, presentation, risk factors, and management of PTLD in KTRs.

**Introduction**

Posttransplant lymphoproliferative disorder (PTLD) is a feared complication following transplantation. The incidence of PTLD in kidney transplant recipients (KTRs) increased in the 1980s and 1990s, but has decreased since approximately 2000. The risk of developing PTLD is increased in KTRs: the lifetime risk for pediatric KTRs is 29 times higher and for adult KTRs 8 times higher than in the general population. A recent study demonstrated that the cumulative cancer incidence was increased 20-fold, with highest risk in the first year posttransplant but remaining increased beyond 10 years. PTLD was the predominant cancer (77%) in this population, with an adjusted hazard ratio of 137.6 compared with a nontransplant pediatric cohort. In an analysis of more than 100,000 patients who received a primary kidney transplant during 2000-2009, the 5-year incidence of PTLD was found to be 0.84%. In a seminal study, Grulich et al demonstrated that the risk for cancer in people with HIV/AIDS and transplant recipients were similar, mainly so for cancers with a known infectious cause. In contrast, most common epithelial cancers did not occur at increased rates.

Transplant registries are important sources of epidemiologic data because the large number of patients improves statistical power. Data linkage between transplant databases and large-scale cancer registries allows for robust data collection and analyses. Smaller single-center or multicenter studies can also have value, as illustrated by a Danish population-based cohort study that included all KTRs during a 20-year period at 2 large transplant centers. For all patients, pathology files were reviewed to identify possible previously unrecognized PTLD cases. Using this approach, the PTLD incidence was higher than observed in registry data (5.2 cases per 1,000 patient-years) and bimodally distributed, with the highest rates in the first year and then beyond 10 years posttransplant.

**Pathophysiology**

A detailed review of the pathophysiology of PTLD is beyond the scope of this review. Briefly, PTLD represents a spectrum of abnormal lymphoproliferations. Despite the strong association between Epstein-Barr virus (EBV) and PTLD, a significant number of PTLD cases are not EBV-associated. In EBV-positive PTLD, EBV infects circulating B cells, resulting in the coordinated expression of EBV proteins, including primary latent membrane proteins (LMP1, 2A-B) and EBV nuclear antigens (EBVNA1, 2, 3A-C;Fig 1). In EBV-negative PTLD, a number of hypotheses have been put forward as possible pathogenic mechanisms, such as “hit-and-run” EBV infection, other infectious agents, and chronic immune activation triggered by the allograft. Recent evidence suggests that the pathophysiology of EBV-positive and -negative PTLD differs, as genomic analysis suggests that EBV-negative PTLD is very similar to sporadic lymphoma in immunocompetent individuals and often contains mutations in the protein TP53. Another interesting hypothesis is that the microenvironment may differ between EBV-positive and -negative PTLD, impacting lymphomagenesis. A small subset of PTLD is T cell–derived; this type is not EBV-driven and typically has a late onset.

**Presentation and Diagnosis**

PTLD following kidney transplantation is predominantly of host origin. Whereas PTLD incidence in adults exhibits a bimodal pattern, pediatric PTLD overwhelmingly occurs in the first year posttransplantation with a long tail.
16 In a large French registry report including 500 patients with PTLD, the gastrointestinal tract was the organ system most commonly involved, with diarrhea, abdominal pain, and (sub)obstruction as the main clinical presentation.17 Clinical features seem to be different when comparing early- and late-onset PTLD. Early-onset PTLD tends to be EBV-driven and often involves the allograft. In contrast, late-onset PTLD often is EBV-negative and involves different extranodal organs.3 Although there is a decrease in the risk of early PTLD, the risk of late PTLD is prolonged, possibly as a result of improved survival of KTRs.18 This is consistent with the fact that higher recipient age is associated with late-onset PTLD.1,3

Currently, PTLD classification is based on the World Health Organization 2017 criteria, describing 4 major subcategories based on morphologic and immunohistochemical characteristics (Table 1). These categories range from (EBV-driven) nondestructive lesions over polyclonal lymphoproliferative disorders to frank monoclonal lymphomas resembling the broad spectrum of all subtypes of lymphomas occurring in immunocompetent persons.17,19 However, this classification clearly needs refinement, as many aspects (eg, EBV association) are not taken into account. The diagnostic workup when there is a suspicion of PTLD includes positron emission tomography (PET) combined with computed tomography (CT) and directed biopsy (bone marrow or lymph node) to make a histopathologic diagnosis (Fig 2).

**Risk Factors**

Although several risk factors for PTLD have been identified, different studies have reported conflicting information in this regard. This is probably related to variations among
study populations (age and race/ethnicity), study periods, EBV prevalence rates, and duration of follow-up. Risk factors also differ between early- and late-onset PTLD. For early-onset PTLD, EBV infection/reactivation and possibly induction therapy are the most important risk factors; for late-onset PTLD, the immunosuppressive state and recipient age are important risk factors.

### EBV Status

More than 50% of PTLD cases are EBV-related, with donor/recipient mismatch (EBV-positive donors and EBV-negative recipients) associated with an increased risk of this complication. Using the Organ Procurement and Transplant Network/United Network for Organ Sharing (OPTN/UNOS) database, Sampaio et al demonstrated that

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Table 1. World Health Organization 2017 Classification of PTLD and Main Characteristics

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<thead>
<tr>
<th>Characteristic</th>
<th>PTLD Classification</th>
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<tr>
<td></td>
<td>Polymorphic</td>
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<tr>
<td>Underlying architecture</td>
<td>(Partially) preserved</td>
</tr>
<tr>
<td></td>
<td>Not preserved</td>
</tr>
<tr>
<td>Cells</td>
<td>Plasma cells, small lymphocytes, immunoblasts</td>
</tr>
<tr>
<td>IHC</td>
<td>No diagnostic value</td>
</tr>
<tr>
<td>EBV</td>
<td>100%</td>
</tr>
<tr>
<td>Clonality</td>
<td>Usually no</td>
</tr>
<tr>
<td>Oncogenic mutations</td>
<td>No</td>
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</tbody>
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Table is based on information in Swerdlow et al. Abbreviations: BLCL, B cell lymphoma; c-MYC, c-myelocytomatosis; DLBCL, diffuse large B cell lymphoma; IHC, immunohistochemistry, N-RAS, neuroblastoma RAS; PTLD, posttransplant lymphoproliferative disorder.

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**Figure 2.** Natural history of PTLD. Kidney transplant recipients receive immunosuppressive therapy to prevent allograft rejection that includes induction (consisting of high-dose glucocorticoids and T cell–directed antibodies) and maintenance therapy (most often consisting of a combination of low-dose glucocorticoids, CNIs, and antimetabolic agents). In addition, when allograft rejection occurs posttransplant, additional immunosuppression is administered. Posttransplant, primary EBV infection or reactivation of EBV infection can result in B cell proliferation. Progression to overt lymphoma occurs when additional genomic aberrations accumulate (in particular in EBV-negative PTLD). EBV nucleic acid testing (NAT) should be performed in EBV-naive KTRs, and RIS should be considered when increasing EBV viral load is detected. If this strategy fails or is not performed, PTLD can develop. In the diagnostic workup of PTLD, a biopsy of a suspected lesion (for pathological classification according to the World Health Organization 2017 classification) and staging are necessary. The treatment consists of RIS and (in most cases) antilymphoma treatment (often including rituximab). After completion of treatment, RIS should be continued even though this poses a risk for graft rejection. When progression to end-stage graft failure occurs, recent data suggest that repeat transplantation is feasible in patients with a history of PTLD.
this EBV donor/recipient mismatch, compared with transplants in which donor and recipient were EBV-negative, was associated with 35% and 42% increases in PTLD incidence in deceased-donor and living-donor kidney transplantation, respectively. Primary EBV infection posttransplant is a major risk factor for EBV-associated early-onset PTLD. Limited data also suggest pretransplant EBV seronegative status as a risk factor for some late-onset cases. For this reason, the American Society of Transplant and KDIGO (Kidney Disease: Improving Global Outcomes) recommend EBV viral load monitoring in pretransplant EBV-seronegative patients receiving donor organs that are seropositive (intensive monitoring, weekly to biweekly for 1 year) or seronegative (less frequent monitoring, monthly).20,21

Human Leukocyte Antigen Status and Panel Reactive Antibodies

Different human leukocyte antigen (HLA) class I and II alleles have been associated with a risk of PTLD following solid organ transplantation: HLA-A26, -B18, -B21, and -B40 with an increased risk; HLA-A3 and -DR7 with a decreased risk. The effect of HLA on PTLD risk seems to be (partially) mediated by the association between HLA alleles and EBV status; the frequency of HLA3 is decreased in EBV-positive PTLD, and the frequency of HLA-B18 is increased in EBV-negative PTLD. Recently, it was reported that HLA-A1 is associated with an increased, and HLA-A2 with a decreased, risk of EBV-positive Hodgkin lymphoma. The mechanism behind the influence of HLA on PTLD risk is probably related to the efficiency of EBV-derived antigen presentation and control of latent EBV infection of different HLA types. Peak panel reactive antibody levels are also related with PTLD risk, and this is probably mediated by an increased risk of rejection (and higher cumulative immunosuppression dosage).22

Patient- and Transplant Organ–Related Factors

An analysis from the Australian and New Zealand Dialysis and Transplant Registry (ANZDATA) demonstrated that, compared with recipients of living-donor kidneys, recipients of expanded-criteria donor kidneys were at an increased risk of PTLD (adjusted hazard ratio, 2.72), possibly due to an enhanced systemic inflammatory response increasing cancer risk and the fact that expanded-criteria donor kidneys are preferentially allocated to older patients. In addition, older recipient age is also a risk factor for development of cancer and PTLD in particular, probably due to immune senescence leading to increased cancer risk.1

Immunosuppression

Overview

The increased cancer risk following transplantation can largely be attributed to an immunodeficient state, with risk for PTLD related to the amount of immunosuppression used. Besides immunosuppression given posttransplant, immunosuppression administered pretransplant has been also been demonstrated to be a risk factor for PTLD.26 It is very difficult to discern the precise contribution of specific immunosuppressive drugs, given that most patients receive induction therapy and a combination of maintenance agents. It is likely that the overall immunosuppressive state (and not a specific immunosuppressive agents) predominates.

Antithymocyte Induction Therapy

Conflicting results have been published regarding the association of rabbit antithymocyte globulin (rATG) induction therapy and risk of PTLD. Two studies found a higher risk in patients with versus without rATG treatment,27,28 whereas one found no significant association.29 This apparent difference is probably due to differences in the study cohorts: in Europe, rATG was used in historically earlier periods (ie, before the 2000s) and at higher doses, whereas, in the United States, the use of rATG gained momentum only after the year 2000. Second, dosing of rATG decreased substantially over time (it was markedly higher in the 1980s, with a total dose of 14 mg/kg, vs 6 mg/kg now). In a systematic review by Marks et al,10 a dose effect of rATG on PTLD risk was noted, as KTRs receiving less than 7.5 mg/kg (5 days of 1.5 mg/kg) had a lower rate of PTLD than those receiving more than 7.5 mg/kg (0.80% vs 1.27%).30 However, this effect was not statistically significant.30 This is supported by 2 Cochrane analyses in lung and liver transplant recipients in which no difference in the rate of PTLD was observed between patients given any T cell antibody induction (including rATG, equine antithymocyte globulin, or antilymphocyte globulin) versus no induction.31,32 rATG is also used to treat allograft rejection episodes, and recipients receive a substantial additional immunosuppressive load in this setting. In an ANZDATA analysis, Lim et al demonstrated that treatment for rejection with T cell–depleting antibody (antithymocyte globulin, antilymphocyte globulin, or muromonab-CD3) was associated with higher rates of malignancy than in patients with no rejection (adjusted hazard ratio, 1.42; \( P = 0.039 \)).33 However, there was no statistical comparison with patients with rejection treated without T cell–depleting antibody.33 In conclusion, there is no increased risk with the current rATG dosing used for induction therapy. Whether rATG dosing used to treat rejection is associated with an increased PTLD risk is uncertain at this time.

Anti–Interleukin 2R Antagonist

In an analysis of the OPTN/UNOS database, there were no differences in the incidence of PTLD within 2 years of transplantation between no induction therapy (0.43%) or induction with basiliximab (0.38%), daclizumab (0.33%),
or alemtuzumab (0.37%). In another ANZDATA-based analysis, induction with interleukin 2R antibody was not associated with PTLD in recipients aged <20 years, in contrast to other induction agents.

**Calcineurin Inhibitors**

Introduction of calcineurin inhibitor (CNI) immunosuppression was associated with a significant increase in the risk of non-Hodgkin lymphoma. Treatment with tacrolimus compared with cyclosporine has been associated with an increased risk of PTLD development in some, but not all, studies.

**Antimetabolites**

In a large population-based cohort study, high doses of azathioprine were associated with increased PTLD risk in solid organ transplant recipients, whereas mycophenolate mofetil does not affect the risk for PTLD, possibly because of its antiproliferative and apoptotic effects.

**Mammalian Target of Rapamycin Inhibitors**

Mammalian target of rapamycin (mTOR) inhibitors are also believed not to impact PTLD risk, and some data even suggest that they potentially reduce PTLD risk. In a prospective registry-linked study in KTRs experiencing solid-organ and hematologic malignancies, CNI therapy was stopped and switched to rapamycin. The results of this trial suggested the potential clinical antitumor effects of mTOR inhibition, though it is hard to completely separate the antitumor effect from the lower-potency immunosuppression effect of mTOR inhibitors compared with CNIs. Despite these promising results, caution remains required given that other trials showed an association between mTOR inhibition maintenance therapy and increased PTLD risk and a meta-analysis demonstrated higher mortality in solid organ transplant recipients receiving mTOR inhibitors.

**Belatacept**

For the costimulation blocker belatacept, PTLD risk appears similar to that seen under CNI therapy, but, of note, belatacept is contraindicated in EBV-seronegative recipients based on initial reports of 2 large phase 3 trials in which PTLD was mainly seen in EBV-negative KTRs (BENEFIT and BENEFIT-EXTENT). The 7-year follow-up data of BENEFIT, however, demonstrated only 1 additional PTLD case.

**Conclusions**

Overall, data suggest that it is the cumulative immunosuppression dosage, rather than specific immunosuppressive agents, that contributes to the well-established decreased or increased PTLD risk.

**Management of PTLD**

**Prevention in High-Risk Patients**

Because EBV plays a pivotal role in the pathogenesis of PTLD in a significant proportion of patients, antiviral treatment and EBV-specific cytotoxic T lymphocytes have been evaluated to prevent PTLD. In some transplant centers, antiviral agents to prevent CMV infections are administered to KTRs, with data suggesting they lower the rate of EBV-associated PTLD. Acyclovir and ganciclovir have been suggested to have a preventive effect on early PTLD in KTRs, but this was not confirmed in a meta-analysis. In another preventive strategy, encouraging results with favorable toxicity profiles have been seen with prophylactic and preemptive administration of EBV-specific cytotoxic T lymphocytes. Few studies have suggested that preemptive reduction in immunosuppression (RIS) or administration of rituximab in transplant recipients with high EBV load results in a reduced incidence of PTLD. Although this is common practice in many transplant centers, it is based on expert opinion, and current guidelines recommend preemptive interventions only in patients who are seronegative pretransplant, with RIS as the preferred intervention in case of a increasing EBV viral load. There are currently no studies in KTRs examining differing risk of PTLD depending on viral load monitoring and the presence or absence of RIS. Furthermore, there is a difference in PTLD risk that depends on whether the increasing titer is related to primary EBV infection or EBV reactivation. We recommend RIS only in KTRs experiencing primary EBV infection.

**Treatment of Established PTLD**

The treatment of PTLD is very much dependent on morphologic subtype. Whereas some subtypes can be treated with RIS alone, other subtypes require additional aggressive immunochemotherapy, radiation therapy, surgery, or a combination thereof. The cornerstone of PTLD treatment is RIS. Current recommendations include reducing CNI dose (targeting 50% reduction of trough levels), discontinuing antimetabolites, and continuing steroids if possible. The role of antiviral therapy in the treatment of PTLD has been very controversial, in part because EBV-driven lymphomas do not express EBV thymidine kinase and/or EBV protein kinase, which would be the targets of nucleoside analogues. For CD20-positive PTLD, in particular diffuse large B cell lymphoma, RIS followed by rituximab has become the standard of care, mainly based on results of the prospective phase 2 multicenter PTLD-1 trial initiated to assess efficacy and toxicity of sequential treatment with rituximab and CHOP chemotherapy. Because response to rituximab predicted overall survival, the trial was subsequently amended to introduce the concept of risk-stratified sequential treatment according to the response to rituximab, if complete remission after 4 administrations of rituximab,
no chemotherapy was added; in the case of no complete remission, CHOP chemotherapy was added). There is currently no evidence that upfront treatment of EBV-negative and EBV-positive PTLD should be different, as the prognosis seems to be similar, and, in the PTLD-1 trial, EBV association was not found to be a significant factor for overall survival or time to progression. However, increased availability of third-party EBV-specific cytotoxic T cells (CTLs) might lead to future differences in treatment between these subgroups in de novo PTLD and in the relapsed/refractory setting. For particular subtypes of PTLD (eg, plasma cell neoplasms, Hodgkin lymphoma, primary central nervous system lymphoma), chemotherapy remains the cornerstone of treatment, combined with rituximab if CD20 expression is present.

New Treatment Options

Given the poor prognosis of patients with PTLD in whom first-line therapy fails, and taking into account increased toxicity in transplant recipients, new therapies combining high efficacy and low toxicity have emerged as an urgent medical need. Although very promising new treatment options have been observed in case reports and very small case series, caution is warranted to maintain balance between tumor control and risk of rejection.

Brentuximab Vedotin

Brentuximab vedotin is an antibody-drug conjugate combining a CD30 monoclonal antibody with the microtubule-disrupting agent monomethyl auristatin E that has shown impressive results in relapsed/refractory CD30-positive lymphomas in immunocompetent patients and an acceptable toxicity profile. Because approximately 70% of PTLDs express CD30 on their surface, brentuximab vedotin may become an attractive treatment in patients with PTLD in whom first-line therapy fails.

Small Molecules

Small molecules targeting B cell receptor signaling and other intracellular pathways have emerged as important therapeutic targets in the majority of B cell lymphoma subtypes. Although their use in PTLD has been very limited, there seems to be a strong in vitro rationale in PTLD as well. In addition, some of these molecules, including the Bruton tyrosine kinase inhibitor ibrutinib, may also be effective in graft rejection.

Checkpoint Inhibition and Chimeric Antigen Receptor T Cells

The use of therapeutic immunotherapy is rapidly growing in oncology in general and in treatments of lymphomas in particular. The potential use of checkpoint inhibition in patients with PTLD has been fueled by the high expression of PD-1 (programmed cell death 1 protein) and PD-L1 (programmed cell death 1 ligand 1) in PTLDs, in particular in EBV-positive cases, which are mainly driven by 9p24.1 gain/amplification. However, switching on the immune system may cause a substantial risk for graft rejection, and this may also complicate the use of chimeric antigen receptor T-cell (CAR-T) therapy, given the potentially impressive cytokine storm associated with this therapy. Krishnamoorthy et al recently reported on the use of CAR-T in solid organ transplantation–related PTLD (including 2 KTRs). All patients experienced significant immunologic side effects, and none showed a response to the treatment. We strongly recommend the use of these treatments only in prospective clinical trials.

EBV-Specific Cytotoxic T Cells

Although the new treatment options described above seem to provide the most benefit for EBV-driven PTLD, their potential use is not restricted to EBV-positive cases. This sharply contrasts with the most promising new tool in PTLD treatment, the use of EBV-specific CTLs. Of course, their therapeutic use is restricted to patients with EBV-positive PTLD. Following initial small pilot trials with autologous (solid organ transplantation) and donor-derived allogeneic (hematopoietic stem cell transplantation) EBV-specific CTLs, further expansion was hampered as a result of practical and logistical reasons. To provide more rapid access, the use of partially HLA-matched EBV-specific CTLs from healthy donors was explored. These so-called third-party donor-derived CTLs can be delivered “off the shelf” in an acceptable time frame to the patient. The largest single-center trial yet was published recently, in which 46 patients with rituximab-refractory PTLD following hematopoietic stem cell transplantation or solid organ transplantation were treated with these cells. Complete or sustained partial remission was achieved in 54% of solid organ transplant recipients, with an excellent toxicity profile. A multicenter, open-label phase 3 trial of tabelecleucel for hematopoietic stem cell transplantation– and solid organ transplantation–associated PTLD after failure of rituximab is presently ongoing (ALLELE study; ClinicalTrials.gov identifier NCT03392142).

Outcome

In general, the prognosis of PTLD following kidney transplant is inferior to the prognoses of immunocompetent patients with diffuse large B-cell lymphoma, with 5- and 10-year survival rates of 53% and 45% in KTRs, respectively. In an ANZDATA-based analysis, Francis et al demonstrated that KTRs with PTLD experienced poorer 10-year patient survival, with excess mortality occurring only in the first 2 years posttransplant. Bone marrow disease and cerebral lymphoma were risk factors for death. PTLD did not confer an excess risk of graft loss. The incidence of PTLD among patients who are EBV-seropositive pretransplant is lower than in KTRs who acquire primary EBV infection posttransplant. In a recent study, L’Huillier et al demonstrated that, compared with patients who acquire EBV after solid organ transplantation, EBV-seropositive
patients developed PTLD later after transplant, with a tendency for higher mortality rate. The outcome of PTLD in KTRs has clearly improved as a result of the introduction of more uniform treatment protocols, improved supportive care, and increased awareness and use of PET combined with CT in staging and response monitoring. The cause of death is primary lymphoma/treatment-related, but late mortality due to infections and secondary malignancies is of particular concern in this population.

In recent years, several risk factors have been identified. These risk factors include classic factors such as older age, advanced disease, poor performance status, increased lactate dehydrogenase levels, low albumin levels, and central nervous system invasion. As with aggressive lymphomas in immunocompetent patients, the International Prognostic Index has been established as a good predictive tool for survival in PTLD. The response to rituximab monotherapy has also been identified as a predictor of overall survival in the PTLD-1 trial in patients with CD20-positive PTLD after solid organ transplant receiving sequential therapy with rituximab and CHOP chemotherapy. As mentioned before, EBV status was not found to be a risk factor for outcome in the PTLD-1 trial.

Given the need for RIS, KTRs are at risk of graft loss following diagnosis of PTLD. In a large French cohort study of 500 patients, acute rejection occurred in 5% following diagnosis and treatment of PTLD. In another French cohort study, multivariate analysis found that an estimated glomerular filtration rate less than 30 mL/min per 1.73 m² at diagnosis, acute rejection following RIS, and the absence of CNI as maintenance immunosuppression were independent risk factors for allograft loss. Thus, maintaining CNI at a reduced dose after the diagnosis of PTLD seems safe and may even improve kidney graft outcome. In addition, the immunosuppressive effect of CHOP chemotherapy and, to a lesser extent, rituximab allows sufficient RIS without compromising allograft function. Repeat transplant after PTLD appears to be an option after complete remission for 1 year, even though a recent registry analysis showed an increased incidence of PTLD after repeat transplant in patients with a history of PTLD versus those without (2.8% vs 0.8%, respectively).

Conclusions

PTLD is a feared complication following kidney transplantation. EBV infection is an important risk factor for PTLD development even though 40% of cases are EBV-negative in modern series. The overall level of immunosuppression seems to be an important driver for the increased risk of PTLD in KTRs. Older lymphocyte-targeting monoclonal antibodies and tacrolimus have been specifically identified to increase PTLD risk in some studies. RIS is commonly accepted as a first step in prevention and treatment of PTLD. In recent decades, outcomes in patients with PTLD have improved because of the introduction of more uniform treatment protocols, improved supportive care, and increased awareness and use of PET/CT in staging and response monitoring. Several novel therapeutic agents are currently being evaluated in the management of PTLD. Finally, repeat transplant appears to be an option after prolonged complete remission.

Article Information

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