To the editor:

Does peritransplantation use of rituximab reduce the risk of EBV reactivation and PTLPD?

A recently published study evaluated 26,901 allogeneic stem cell transplant (allo-SCT) recipients to define the risk factors for posttransplantation lymphoproliferative disorders (PTLPD).1 PTLPD developed in 127 (0.47%), with more than 80% of cases occurring within the first year after allo-SCT. The authors identified 4 high-risk factors associated with increased risk for PTLPD. Patients with no risk factors (80.6%) had a cumulative incidence of 0.2% versus 8.1% for patients in whom 3 or more risk factors were present (0.64%). The risk associated with antithymocyte globulin (ATG) use was not analyzed in this study; however, with the recent trends of using lower ATG doses and close Epstein-Barr virus (EBV) monitoring with preemptive therapy for EBV reactivation, one would expect lower risk for development of PTLPD.

The prevalence of PTLPD in patients previously treated with rituximab is not known. Landgren et al1 observed a lower risk of PTLPD when T-cell depletion methods used removed both T and B cells (CAMPATH-1 and elutriation) compared with those depleting T cells only. Rituximab is commonly used for treatment of B-cell malignancies and has been shown to be effective as a preemptive therapy for EBV reactivation.2 In our experience, when patients were previously treated with rituximab, EBV reactivation was not observed (n = 38; January 2006 through January 2009). This includes the use of standard doses of rituximab-containing conditioning regimen followed by matched donor allo-SCT (n = 4) or prior rituximab for B-cell hematologic malignancies followed by matched related (n = 20), unrelated donor (n = 11; 6 patients received rabbit ATG 7.5-10 mg/kg), or cord blood (n = 3) transplantation. Not surprisingly, this was true even in 8 patients with 3 high-risk factors (unrelated donor, ATG use, age ≥ 50 years) for PTLPD (rituximab-containing regimen = 3; prior rituximab = 5) as defined by Landgren et al.1 All patients underwent allo-SCT on standard of care or institutional review board–approved protocols and signed data consents. Informed consent was provided according to the Declaration of Helsinki. Interpretation of our results is limited by the small number of patients in our series.

Vienna et al3 showed no PTLPD following a single dose of rituximab (150 mg/m²), rabbit-ATG (10 mg/kg) and 6 months of immunosuppression for patients receiving multivisceral transplantation. In this series, nearly half of the patients received additional immunosuppression for the graft rejection (high-dose steroid or additional ATG or CAMPATH-1). It is expected that the reconstituted B-cell population after a transplant remains significantly depleted of memory CD27+ B cells for as long as 2 years after single dose of rituximab.4 It would be interesting to see how many EBV reactivations and PTLPDs have been observed after rituximab containing conditioning regimen for B-cell malignancies from a larger database.3 Rituximab infusion given 2 months after total lymphoid irradiation (TLI)-ATG showed excellent disease control with minimal graft-versus-host disease (GVHD) without any detrimental effects on engraftment or infection and no EBV reactivation reported.4 The European Group for Blood and Marrow Transplantation (EBMT) Working Party on Severe Aplastic Anemia (SAA) proposed adding rituximab on day +5 of their fludarabine, cyclophosphamide, low-dose total body irradiation (TBI), and ATG regimen for unrelated donor transplants in acquired SAA.7

Rituximab, with (if GVHD is present) or without donor lymphocyte infusion (DLI), has been used for persistent disease after allo-SCT for chronic lymphocytic leukemia (CLL) with excellent results.5,8 In addition to benefits of decreasing risk of GVHD and better disease control in patients with B-cell malignancies, one would expect lower EBV reactivation and PTLPD after these regimens. If the risk of EBV reactivation and the possible development of PTLPD is reduced in patients treated with rituximab, then we will need ask these questions: (1) How should we monitor high-risk patients treated with rituximab? (2) Will we see more non–B-cell PTLPD?

Studies have shown that rapamycin, a potent immunosuppressive drug, inhibits growth of EBV-transformed B lymphocytes and causes programmed cell death in B-lymphoma cells.9-10 A recent report describes 2 patients with PTLPD successfully treated with rituximab and rapamycin after renal transplantation.11 Rapamycin has been shown to be effective GVHD prophylaxis after allo-SCT;12 however, the prevalence of PTLPD was not reported. These observations suggest consideration of a clinical trial using a conditioning regimen incorporating rapamycin and lower doses of rituximab for GVHD prophylaxis in high risk patients for PTLPD and GVHD, especially older patients receiving unrelated or mismatched transplantation with ATG.

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References


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