13. Post-transplant Lymphoproliferative Disorder

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13.1 Overview of PTLD


- Comprehensive review of PTLD after solid-organ transplant and hematopoietic stem-cell transplant. Topics include epidemiology, risk factors, pathogenesis, clinical presentation, diagnosis and summary of treatment options.


- Case-series describing five late-onset PTLDs with rare histological features and multiorgan involvement.


- Nationwide cohort study based on data from the multicenter nationwide observational Swiss Transplant Cohort Study (STCS) to describe the clinical characteristics of PTLD cases after SOT and to assess the effect of rituximab therapy and the use of antiviral prophylaxis on PTLD occurrence. Total of 4765 SOT patients (7% kidney, 22% liver, 9% lung, 8% heart, 5% combined) with 57 cases of PTLD. 86% of PTLD cases were EBV positive. The overall PTLD incidence was 2.39 per 1000 person-years. Incidence rates for EBV+ PTLD at 1, 2, and 3 years post-transplant were 3.51, 2.24, and 1.75/1000 person-years and 0.44, 0.25, and 0.29/1000 person-year for EBV− PTLD. Majority of SOT patients receiving rituximab were kidney transplant recipients (95%). Among them, 88% received rituximab as induction therapy. The mean PTLD-free survival time at 9 years of follow-up was significantly shorter (0.104 years [95% CI 0.077–0.131]). Patients not receiving rituximab induction had a significantly shorter mean PTLD-free survival time at 9 years follow-up (0.067 years [95% CI 0.039–0.096]).


- Single center, retrospective study was conducted to compare the clinical, biological and histological features and outcomes of PTLD after solid organ transplant and hematopoietic stem cell transplant. Found that PTLD had an earlier onset in patients with allo-HSCT compared to
SOT (4 vs 64 months, p<0.0001). Median overall survival after four years was 32% (95% CI, 22-48) in SOT and 10% (95% CI, 2-49) in allo-HSCT recipients, p = 0.002.

- Comprehensive review of PTLD following solid organ transplant and hematopoietic stem cell transplant with a focus on management. Includes an overview of ongoing clinical trials of novel agents

- A comprehensive review of PTLD in adult transplant recipients, including solid organ transplant and bone marrow transplant.

- Comprehensive review of hematologic cancers, including PTLD, following solid organ transplant.

- Single center study from Alberta evaluating SOT patients of all organs between 1/1/1984 - 12/31/2013 (n=4171) and the characteristics of those who developed PTLD. Multi-organ, small bowel, and thoracic transplants had an increased risk of PTLD (Multi-organ/small bowel: 95% CI 1.5-84; P=0.019; thoracic: 95% CI 1.5-4.5; P<0.001). Epstein-Barr virus seronegative patients had an eight-fold higher risk of PTLD (95% CI: 5.1-13; P<0.001). The risk for PTLD is higher at 1 year post-transplant vs. 10 years post-transplant (HR: 17.1, 95% CI: 8.1 - 35.7 versus HR: 11.5, 95% CI: 7 – 18.8).

- Retrospective review of SOT patients diagnosed with PTLD at a single U.S. center between December 1970 and May 2003. Early PTLD was defined as PTLD that occurs within 1 year post transplant. The authors concluded that patients with early PTLD were likely to be EBV+, CD20+, and more commonly involved the grafted organ.

13.2 PTLD and Epstein - Barr virus

- Retrospective cohort study reporting the characteristics and outcomes of PTLD in the rituximab era with a total of 66 patients with PLTD following SOT at a median follow-up of 9 years. Overall median time from SOT to PTLD was 5.5 years with the longest time to diagnosis in infant transplants; overall survival was a median of 19 years. Response rate in the monomorphic DLBCL was 72% (n = 26) and 92% in polymorphic PTLD (n =12).

Allen UD, Preiksaitis JK. (2019). Post-transplant lymphoproliferative disorders, Epstein-Barr virus infection, and disease in solid organ transplantation: Guidelines from the American Society of
- AST Infectious Disease Community of Practice updated guidelines. Reviews diagnosis, management and prevention of PTLD and EBV syndromes after solid organ transplantation.

13.3 PTLD following cardiac transplant

- Retrospective cohort study investigating the incidence of and risk factors for de novo malignancy after heart transplantation from a single center (Tokyo, Japan), with the correlation of infectious events and de novo malignancy. Further division of malignancy into PTLD group revealed the frequent negative EBV serostatus, CMV positive antigenemia, and occurrence of any viral or GI infections at ≤ 1 year.

13.4 PTLD following liver transplant

- Case report of the first case of refractory BL-PTLD successfully treated using autologous anti-CD19 chimeric antigen receptor (CAR) T cell therapy. Sustained complete remission and manageable cytokine release syndrome were achieved.

13.5 PTLD following renal transplant

- A retrospective review of 8 kidney transplant recipients who developed PTLD and subsequently underwent retransplantation from 1963 to December 2012 at a single U.S. center. After a median follow-up of 62.5 months (range 2-125 months) allograft survival was 87.5% (7 functioning grafts, 1 failed graft from chronic rejection), with no recurrence of PTLD. Three patients died from causes other than PTLD.

13.6 PTLD following intestinal transplant

- A comprehensive review of PTLD in pediatric intestinal transplant recipients in regard to pathology, presentation, and management. Also provides a summary of cases reviewed from the literature.

13.7 Management of PTLD

• Case series reporting outcomes of three SOT patients (one heart, one kidney, one pancreas) with refractory PTLD that received CAR-T therapy. All patients had major complications from CAR-T therapy and eventually expired.


• Multicenter, retrospective study looking at patients (n=155) with DLBCL-type PTLD treated with regimens that included rituximab. Two-year overall survival with rituximab-containing therapy was 63.7% (95% CI 56.6 - 71.1%). No difference in survival between R-CHOP therapy and rituximab primary therapy. Multivariate analysis in 109 patients concluded that baseline IPI score and response to rituximab induction therapy are predictors for overall survival.


• Prospective, multicenter, open-label, phase II trial evaluating 152 CD20+ PTLD patients who failed reduced immunosuppression. All patients received rituximab whereby on day 50, if patients were complete responders they would continue rituximab monotherapy. All others would receive R-CHOP. The study concluded that treatment stratification into rituximab or R-CHOP consolidation on the basis of response to rituximab induction is safe and effective.


• International multicenter open-label phase 2 trial, treatment-naive adult solid-organ transplant recipients diagnosed with CD20-positive PTLD who had failed to respond to upfront immunosuppression reduction received four courses of rituximab (375 mg/m² IV) once a week followed by 4 weeks without treatment and four cycles of CHOP every 3 weeks. In case of disease progression during rituximab monotherapy, CHOP was started immediately. The primary endpoint was treatment efficacy measured as response rates in all patients who completed treatment with rituximab and CHOP, per protocol, and response duration, in all patients who completed all planned therapy and responded. Secondary endpoints were frequency of infections, treatment-related mortality, and overall survival.


• Retrospective review of solid organ recipients diagnosed with PTLD between August 1988 and June 2008 at a single U.S. center. Of 162 adult patients diagnosed, 148 were evaluated. Patients were treated with either reduced immunosuppression (RI) alone (n=67), surgical excision followed by RI (n=30), or other first line therapies with or without RI (n=51). The study demonstrated a 45% response rate from RI alone, with the majority being complete response. There was a 32% acute rejection rate with RI-containing regimens with some requiring a second transplant. Of note, monomorphic PTLD was diagnosed in 63% patients treated with RI alone vs. 39% patients treated with other first-line therapies, implying a selection of patients with monomorphic PTLD for treatment with RI alone (p=0.011). The study also identified the following risk factors for poor response: bulky disease, advanced stage, and older age.

- PTLD guidelines from a joint working group established by the Haemato-oncology subgroup of the British Committee for Standards in Hematology (BCSH) and the British Transplantation Society (BTS). This review details the therapeutic options recommended including reduction in immunosuppression, transplant organ resection, radiotherapy and chemotherapy.


- A multi-center, prospective, phase II study of 16 patients with biopsy-proven PTLD after any organ allograft (excluding lung) transplantation. A sequential approach was used in this study, starting with reduction in immunosuppression, escalating to interferon alpha2b, and finally to chemotherapy. The response rate to reduced immunosuppression was 0/16 complete remission and 1/16 (6%) partial remission. Six of the 16 patients (38%) had documented rejection during the period of reduced immunosuppression. Thirteen patients underwent treatment with IFN alpha with 2/13 (15%) complete remission and 2/13 (15%) partial remission. Lastly, 7 patients proceeded to ProMACE-CytaBOM chemotherapy with 67% complete remission.


- Phase 2 study conducted at 15 French and 4 Belgian centers between May 2000 and December 2001. Forty-six patients with untreated B-PTLD that were not responding to tapering of immunosuppression were included and 43 patients (18 kidney, 11 heart, 7 liver, 4 lung, and 3 heart-lung) were analyzed. Treatment consisted of 4 weekly injections of rituximab at 375 mg/m^2. Immunosuppressive drugs were stopped if possible, or dosage reduced by at least 50% and/or the number of drugs reduced to no more than two. At day 80, 37 (86%) patients were alive and the response rate was 44.2%, including 12 patients with a complete response. The overall survival rate at 1 year was 67%.


- Retrospective review of 11 transplant recipients (4 kidney, 1 heart, 1 kidney-pancreas, 4 single lung, and 1 bilateral lung) at two U.S. centers diagnosed with PTLD treated with rituximab. Immunosuppressive therapy was reduced in dose or discontinued in all patients at the discretion of the managing physician. Three patients received a course of acyclovir. The overall response rate was 64% (6 complete remission, 1 partial remission, 2 progressive disease, and 2 deaths) and 55% complete remission rate.


- A report of a single U.S. center's utilization for rituximab in PTLD as salvage therapy on long term outcomes. The authors found poor response rates and survival rates compared to other studies. The patients in the analysis had a high tumor burden and did not receive surgical interventions prior to rituximab.

- A multi-center, prospective study investigated the use of rituximab in 17 patients with PTLD (5 heart, 4 kidney, 4 lung, and 4 liver) between 1999 and 2002. Patients were treated with four weekly doses of 375 mg/m² of rituximab. Immunosuppressive therapy was reduced in all patients prior to their entry into the study protocol. Complete remission was achieved in 9 patients (52.9%) with a mean duration of 17.8 months; interestingly, these 9 PTLD cases were EBV-associated. The mean overall survival period was 37.0 months with 11 patients still living at the time of publication.


- Retrospective review of 42 adult patients treated with either reduced immunosuppression (RI) with or without surgical resection of all known disease. 63% (19/30) responded to RI alone with multivariate analysis indicating elevated LDH, organ dysfunction, and multi-organ involvement as risk factors for poor responders of RI. At the median follow-up of 147 weeks, 55% of patients were alive with 50% in complete remission.

13.8 Retransplantation following PTLD


- The Organ Procurement and Transplant Network/United Network for Organ Sharing database was reviewed for individuals who developed PTLD and underwent retransplant from 1987 through 2004.