Abstract
Post-transplant lymphoproliferative disorders (PTLDs) are serious, life-threatening complications of transplantation, which represent a heterogeneous group of lymphoproliferative diseases and show a spectrum of clinical, morphologic, and molecular genetic features ranging from reactive polyclonal lesions to frank lymphomas. Polymorphic (P) PTLD are composed of immunoblasts, plasma cells and small and intermediate-sized lymphoid cells that efface the architecture of lymph nodes or form destructive extranodal masses and do not fulfill the criteria for any of the recognized types of lymphoma described in immunocompetent hosts, which shows characteristic clinicopathological features and molecular involvement.

KEYWORDS
Post-transplant lymphoproliferative disorders; lymphoma; B-cell; T/NK cell

Clinics and pathology
Disease
The term "post-transplant lymphoproliferative disorder" or disease (PTLD) was first introduced in 1984 by Starzl (Starzl et al. 1984). PTLDs are serious, life-threatening complications of solid-organ transplantation (SOT) and bone marrow transplantation, and are associated with high mortality. PTLDs represent a heterogeneous group of lymphoproliferative diseases, which show a spectrum of clinical, morphological, and molecular genetic features ranging from reactive polyclonal lesions to frank lymphomas. PTLDs are classified into early lesions, polymorphic, monomorphic, and classical Hodgkin's lymphoma-like PTLD.
P-PTLD shows characteristic clinicopathological features and molecular involvement. P- PTLD are composed of immunoblasts, plasma cells and small and intermediate-sized lymphoid cells that efface the architecture of lymph nodes or form destructive extranodal masses and do not fulfill the criteria for any of the recognized types of lymphoma described in immunocompetent hosts (Swerdlow, et al., 2008. Mucha, et al. 2010.)

Phenotype/cell stem origin
The majority (>90%) of PTLD in solid organ recipients are of host origin and only a minority of donor origin. Donor origin PTLD appear to be most common in liver and lung allograft recipients, and frequently involve the allograft. In contrast, the majority of PTLD in bone marrow (BM) allograft recipients are of donor origin, as would be expected, since successful engraftment results in an immune system that is nearly exclusively of donor origin (Chadbourn, et al., 1995. Swerdlow, et al., 2008). Phenotypically, P-PTLD cases show B cells with or without light chain class restriction and a variable proportion of heterogeneous T cells that sometimes predominate. Light chain class restriction, when present, may be focal, and some cases may
demonstrate different clonal populations in the same or different sites. Cases with clearcut light chain class restriction should be differentiated from monomorphic PTLD. Reed-Sternberg-like cells when present are often CD30+, CD20+ but CD15-. Most cases of P-PTLD contain numerous EBER-positive cells (Swerdlow, et al, 2008. Dunphy CH, et al, 2002).

**Epidemiology**

The incidence of PTLD ranges from 1-3% in renal to 5-20% in lung and intestinal transplantation, related to the type of transplanted organ, intensity of IS, age, and viral infection, etc (Opelz, 2003. Opelz, 1993.) In contrast, the incidence of PTLD after BMT is about 1.0% for recipients from HLA-compatible related donors (lower than that of SOT), but in up to 25% for high-risk patients (Curtis, 1999). However, the field has evolved during the last decade. Hoegh-Petersen et al. found a frequency of 8.1% among 307 allo-HSCT recipients who had also received ATG-based conditioning. Kamani et al. found an overall incidence of 2.3% for post-transplant malignancy (most of which were PTLD) in patients receiving such transplant for primary immunodeficiency disorders. The highest subgroup, those patients with Wiskott-Aldrich syndrome, had a 3.3% frequency.

In our hospital, it is 1.5% (9/585) from August 2002 to October 2006 and about 1% (9/857) from November 2006 to November 2009 after allo-HSCT, respectively. The incidence of PTLD was higher in mismatched or unrelated HSCT group than that of conventional one, 3.4% (7/208), 2.3% (1/44) versus 0/323. It was also higher in patients with conditioning regimen including ATG than those without, 3.4% (9/262) vs. 0/323 (Swerdlow, et al, 2008. Chen, 2013).

**Clinics**

The clinical features of PTLD differ from those of lymphomas observed in the general population. Symptoms may be mild, such as fever, mononucleosis-like syndrome, lymphadenopathy, recurrent infections or severe organ dysfunction. The variable manifestation of PTLD depends on many factors, such as the type of transplanted organ or IS used, histopathology and time elapsed since transplantation. The first year after transplantation is important, in lung recipients, more than 50% of all PTLDs develop during the first post-transplant year. Our data showed that 88.2% of patients (15/17) were diagnosed within 7 months after transplantation (1.5-7 months), and the median interval after transplantation to the diagnosis was 2.5 months (mean 4.7 months, range 1.5-19 months), shorter than that of SOT. The frequent sites of PTLD include GI (jejunum more often than colon), lymph nodes, and central nervous system, different from type to type of transplantation.


**Pathology**

P-PTLD is characterized by effacement of the architecture and full range of B-cell maturation from immunoblasts to plasma cells, with lymphocytes and Hodgkin and Reed-Sternberg (HRS)-like cells. P-PTLD was proposed to separate into polymorphic B-cell hyperplasias and polymorphic B-cell lymphoma, the former composed of a mixture of lymphoid cells with prominent plasmacytoid differentiation and abundant immunoblasts without cytologic atypia, in which necrosis was limited to single cells or small foci, whereas the latter lacking prominent plasmacytoid differentiation with significant cytologic atypia, atypical immunoblasts, and large confluent coagulative areas of necrosis (Knowles, et al, 1995).
**Figure 1.** Polymorphic PTLD. Effacement of the architecture and proliferative lymphoid cells. (HE stain)

**Figure 2.** There is a polymorphic proliferation of immunoblasts, small lymphoid cells and plasma cells, with lymphocytes and HRS-like cells
Figure 3. Full range of B-cell maturation from immunoblasts to plasma cells.

Figure 4. Some cells are positive for CD20.
Figure 5. Some cells are positive for CD3.

Figure 6. Plasma cells are positive for CD38.
Some plasma cells are positive for Kappa. There is no light chain restriction can be seen.
**Figure 9.** The proliferation index of Ki 67 is 95%.

**Figure 10.** The immunoblasts were positive for CD30, variable in staining intensity.

**Treatment**

There is no consensus on the optimal treatment of PTLD. It is generally agreed that three major strategies should be applied: restoration of the recipient's immunity (to limit the EBV infection), elimination EBV and removal of neoplastic B cells. Reduction of IS or even withdrawal remains the first-line treatment. With reduction of immunosuppression, virtually all early lesions regress and generally show good prognosis, whereas half of P-PTLD regress and some will progress, the majority of M-PTLDs do not regress. DLI was effectively used in EBV-associated PTLD after mismatched/haploidentical haematopoietic stem cell transplantation (HSCT). Patients with lymph node

**Prognosis**

The prognosis of PTLD is poor. The treatment of rejection episodes with OKT3 or ATG enhances the PTLD risk in patients who did not receive antibody induction, rejection therapy with OKT3 or ATG adds to the already increased lymphoma risk HLA matching is also a risk factor in the pathogenesis of PTLD, and HLA-B or HLA-DR mismatches especially seem to be critical. The number of HLA mismatches parallels with an increased risk of PTLD (Opelz, et al, 2003. Opelz, et al, 2010).

**Genetics**

Note

P-PTLD are expected to demonstrate clonally rearranged immunoglobulin genes although the clones are less predominant than in monomorphic PTLD. Seventy-five percent of P-PTLD are reported to have mutated immunoglobulin gene variable regions without ongoing mutations and the remainder are unmutated. BCL6 somatic hypermutations may be present as well as aberrant promoter methylation, but other oncogene abnormalities are not detected (Swerdlow, et al., 2008. Capello, et al, 2005).

**References**


This article should be referenced as such: