

Leukaemia Section

Short Communication

Infectious mononucleosis-like PTLD

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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. Infectious mononucleosis (IM)-like PTLT is a kind of early lesions, which shows characteristic clinic-pathological features and molecular involvement.

Identity

Other names
IM-like PTLT

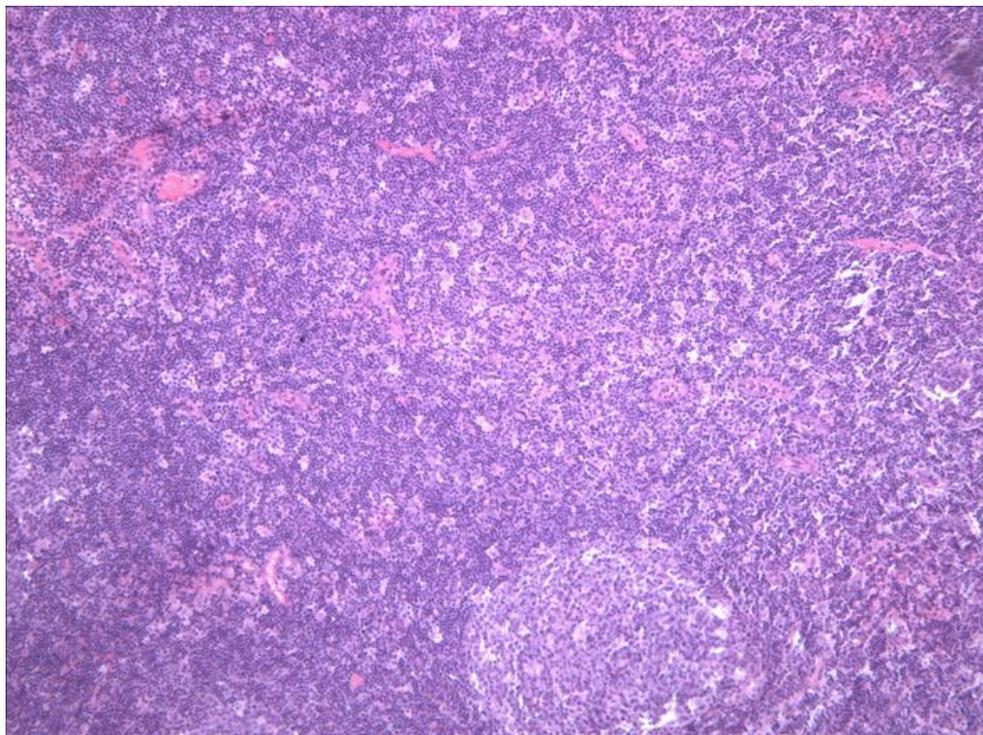


Figure 1. Infectious Mononucleosis-like PTLT: hyperplasia of plasma cells and lymphocytes in interfollicular area, with scattered immunoblasts and reactive follicles. (HE stain)

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, morphologic, 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.

Infectious mononucleosis (IM)-like PTLD is a kind of early lesions, which shows characteristic clinicopathological features and molecular involvement. The early lesions are defined as lymphoid proliferations in an allograft recipient, characterized by architectural preservation of the involved tissue, with preservation of the nodal sinuses or tonsillar crypts, and residual or sometimes floridly reactive follicles in some cases. (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. (Chadburn et al. 1995; Swerdlow et al. 2008)

Phenotypically, IM-like PTLD cases show an admixture of polyclonal B cells, plasma cells and T cells without phenotypic aberrancy. Some cells of which may express CD20, PAX5, CD3, CD5, CD38, CD138, Kappa, Lambda, and the index of Ki67 can be very high (~90%). EBV detected by *in situ* hybridization is usually positive, and EBV-LMP1+ immunoblasts can be seen. (Swerdlow et al. 2008)

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.

Early lesions mostly develop within 1 year after transplantation, and most patients with early lesions affected tonsils, Waldeyer ring, adenoids or lymph nodes. They often show spontaneous regression or regress following reduction in IS, and express EBER or EBV-LMP-1. IM-like PTLDs occur at a younger age than the other PTLD and are often seen in children or in adult solid organ recipients who have not had prior EBV infection. IM-like PTLDs can be fatal (Opelz, 2003; Swerdlow et al. 2008; Johnson, 2006).

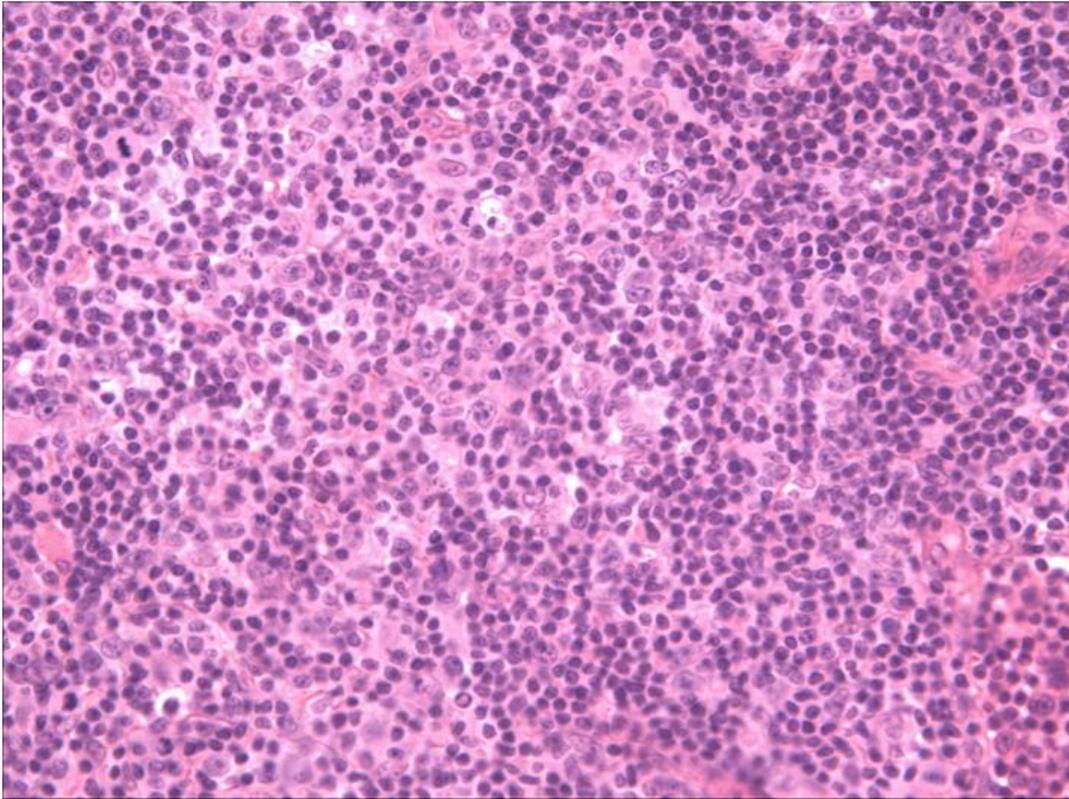


Figure 2. There is a polymorphic proliferation of immunoblasts, small lymphoid cells and plasma cells.

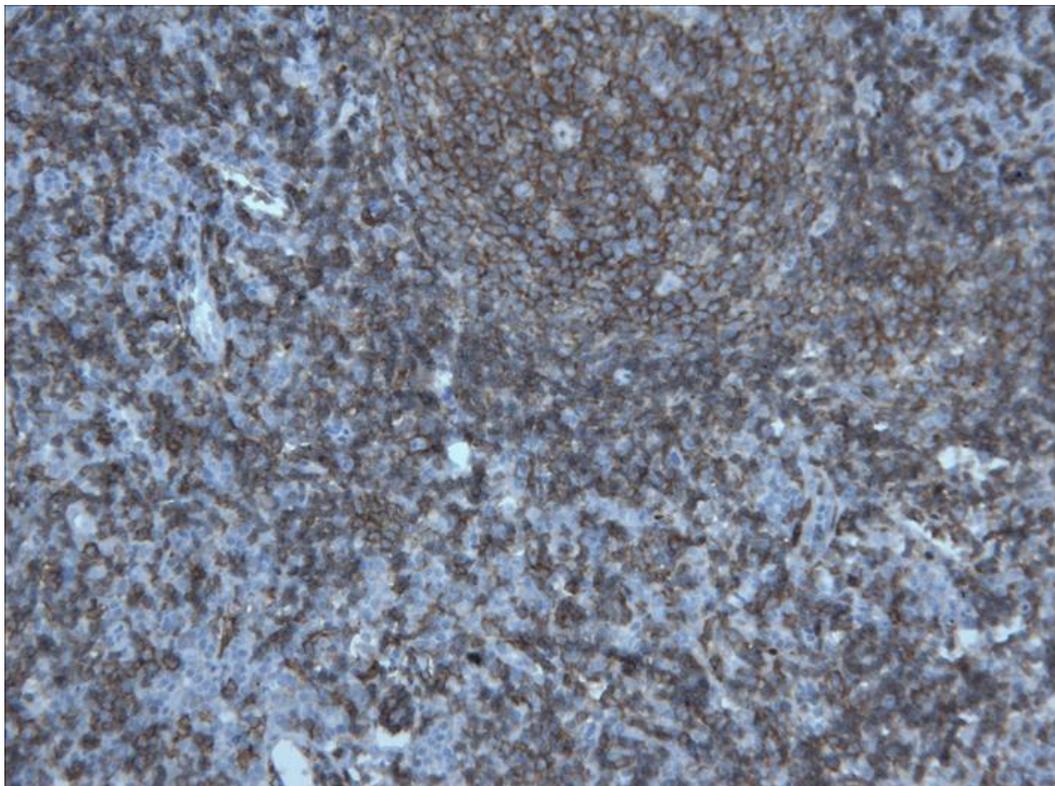


Figure 3. Some cells are positive for CD20, and scattered B cells are shown.

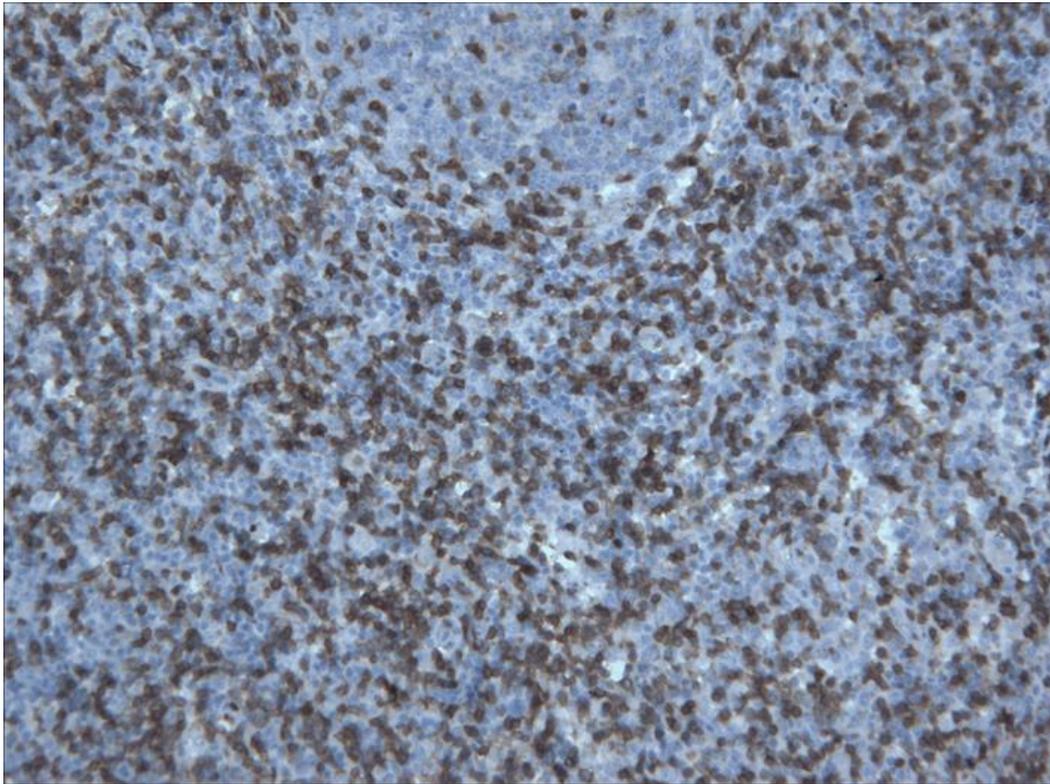


Figure 4. Some cells are positive for CD3

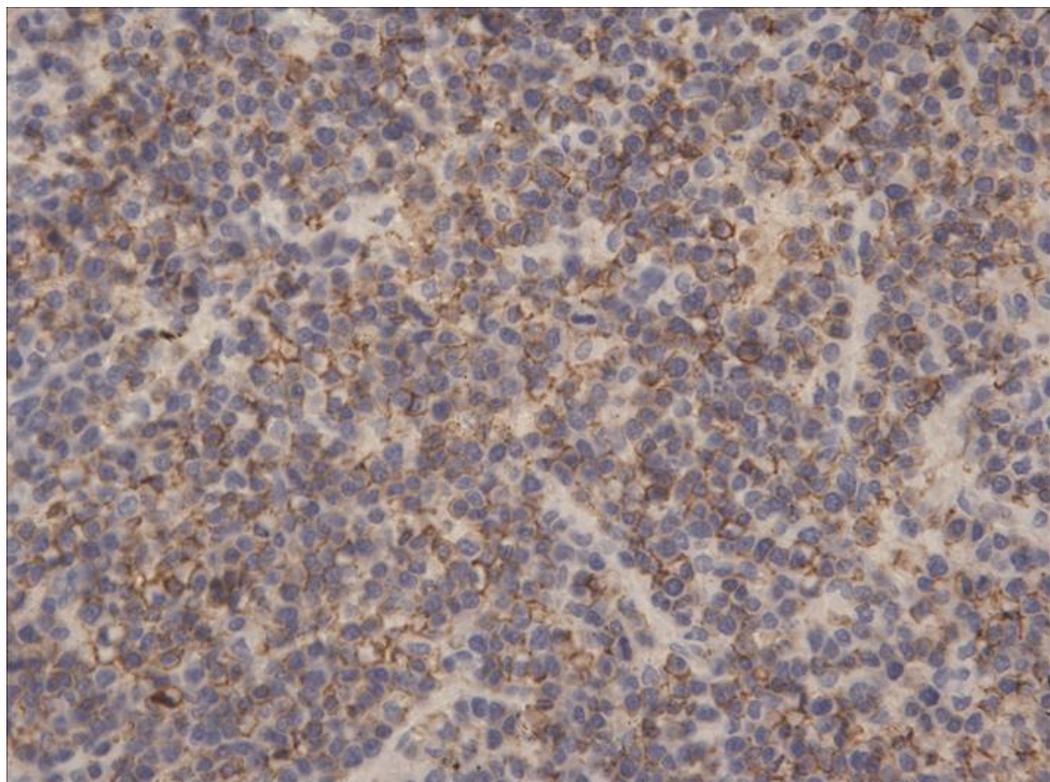


Figure 5. Foci of plasma cells are positive for CD38.

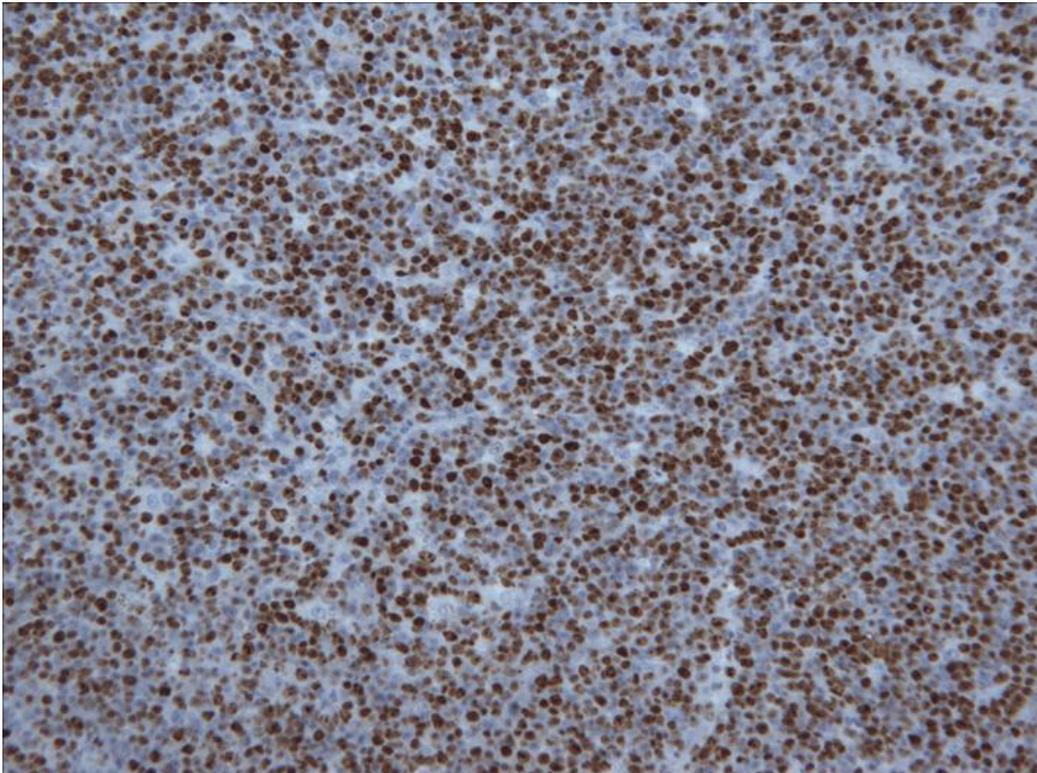


Figure 6. The proliferation index of Ki 67 is 95%.

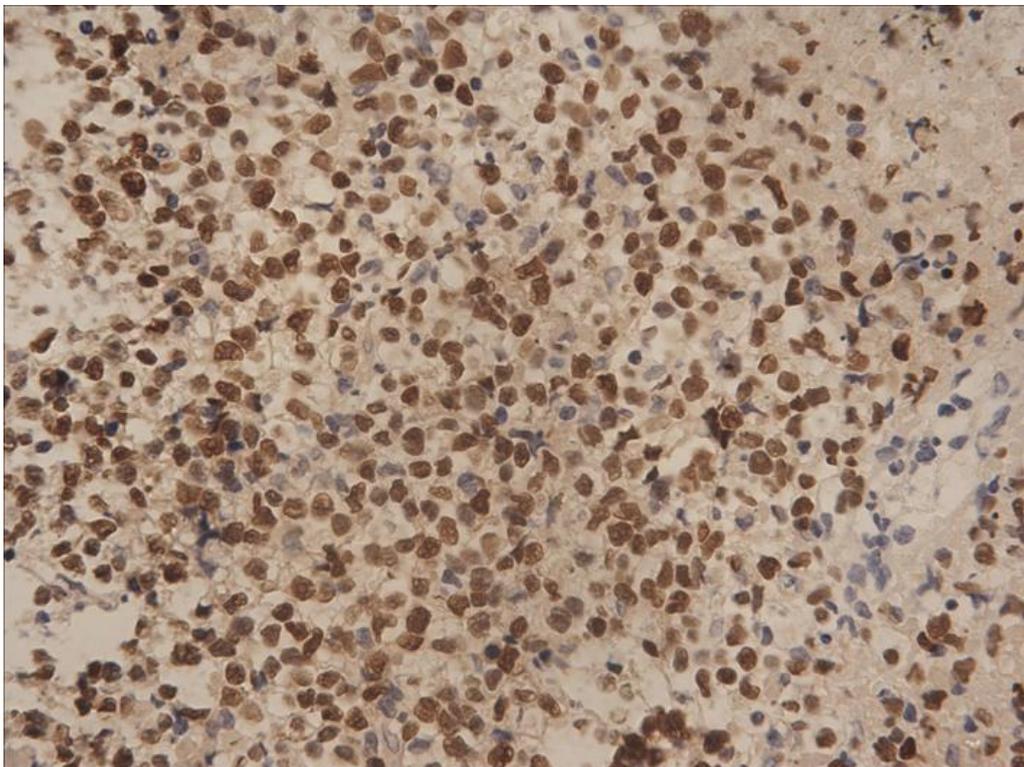


Figure 7. EBER-positive cells are present (in situ hybridization)

Pathology

The underlying lymph node architecture is preserved, which shows hyperplasia of plasma cells and lymphocytes in interfollicular area, with paracortical expansion, scattered immunoblasts and reactive follicles

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 IS, 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 localization have a relatively good outcome, and disseminated disease in contrast has a poor prognosis. (Mucha 2010; Xu 2010)

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 2003; Opelz 2010)

Cytogenetics

Cytogenetics morphological

Some IM-like PTLD may have small monoclonal or oligoclonal populations. The significance of oligoclonality or a small clonal band in these cases is unknown. (Swerdlow et al. 2008.)

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