

## PW1-4

### **Sensing malignancy: Prodromal signs of post-transplant lymphoproliferative disease in pediatric heart transplant recipients**

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**Background:** Post-transplant lymphoproliferative disorder (PTLD) contributes to morbidity and mortality after transplantation. Early and adequate diagnosis can be challenging due to unspecific and heterogeneous clinical presentation. The aim of this review was to determine characteristic prodromal signs of PTLD development.

**Methods:** Medical records of 106 pediatric heart transplant patients at our institution were retrospectively reviewed for PTLD development, their clinical course including B symptoms, lymphoma-like changes in blood cell counts, EBV antibody titers and immunosuppression levels prior to PTLD diagnosis.

**Results:** Between 1990 and 2010 seven of 106 children (6,6%) developed PTLD within five month to fourteen years post heart transplantation (HTx) (mean  $7,7 \pm 5,1$  y). Biopsies revealed polymorphic B cell lymphoma (five), monomorphic diffuse B cell lymphoma (one) and plasmacytic hyperplasia (one). Five of seven recipients diagnosed with PTLD were under one year of age at time of HTx and all but one (6/7) were initially EBV seronegative. Our patients presented from four month to two days before diagnosis with recurrent fever of unknown origin (5/7), decrease in general performance (7/7) and lymphadenopathy (4/7, 4 cervical, 1 submandibular, 2 axillary). Lab results showed rising EBV-antibody titers (5/7, two cases EBV-negative even after PTLD diagnosis), increasing lactate dehydrogenase (LDH) levels up to 447-1072 U/l (4/7) and remarkable dropping in blood cell counts (microcytic anemia and leukopenia, 4/7). Immunosuppression regimen and drug levels showed no relevant changes before PTLD onset.

5/7 cases were treated successfully with reduction of immunosuppression (and/or conversion to everolimus /monotherapy) and chemotherapy (NHL-BFM 95, Ped-PTLD 2005). One case with monomorphic lymphoma showed low response to Rituximab and developed a relapse of PTLD. An older recipient died of pulmonary deterioration during chemotherapy.

**Conclusions:** Tight follow-up with a close look for PTLD prodromal signs in anamnesis and clinical examination like recurrent fever of unknown origin, lymphadenopathy and reduced general condition, is crucial for patients at risk for PTLD, especially in the infant recipient group. Rising EBV-load and correlating changes of blood cell counts and LDH peaks are further hints for a looming PTLD development.