This case concerns a ten month old infant with a ventricular septal defect, failure to thrive, and acute congestive heart failure who was referred to our tertiary care hospital for surgical repair. He was born at 36 weeks and during his four day postnatal hospital course was diagnosed with a ventricular septal defect. After discharge, his second newborn screen demonstrated elevated citrulline which prompted an outpatient genetics referral. The confirmatory testing with amino acid levels was sent, but no genetic microarray analysis was performed. At ten months of age he was put forward for ventricular septal defect closure due to over circulation and failure to thrive. As per our institutional practice, only infants less than one month of age routinely receive irradiated and cytomegalovirus-negative packed red blood cells and plasma for the cardiopulmonary bypass prime.

Therefore, his CPB circuit was primed with plasma and packed red blood cells that were only cytomegalovirus safe. After the primary median sternotomy was performed the thymus was noted to be absent in a patient who had no pre surgical CMA. At this point in the operation, there was concern by the anesthetic and surgical teams regarding the possibility of cytomegalovirus infection, or graft versus host disease from the CPB prime in an athymic patient. The decision was made to reprime a second CPB circuit with CMV negative, irradiated blood and then proceed with the operation. Prior to initiating CPB or any blood product transfusion, a CMA was sent. The VSD was then closed by autologous pericardial patch. He had an uneventful postoperative course, and the CMA did confirm a 22q11 deletion.

Discussion

Established in the 1990’s, The Society of Thoracic Surgery database committee is a nationwide, voluntary and anonymous registry of congenital cardiac cases and outcomes. An IRB was obtained and the STS Congenital Heart Disease database was queried from January 2010- June 2011 to identify children with chromosomal anomalies undergoing procedures involving cardiopulmonary bypass. 26,019 children were identified as undergoing a CPB case during the time period with 3,893 (15.6%) children reported as having a chromosomal anomaly (figure 1). Of the children reported as having a chromosomal anomaly, the sample size was further broken down by age: neonates (0-30 days) 423 (1%), infants (31-365 days) 2,470 (cases) (62%), and child (1-18 years) 955 cases (24%) (Figure 2). The largest group with chromosomal abnormalities reported to the STS CHD database were children with Trisomy 21, with a 9.58% incidence. Other commonly reported chromosomal anomalies included 22q11 deletion syndromes with a 2.2% incidence, children with an unidentified chromosomal defect 2.94%(figure 3). However it is important to note that the STS CHD database is a voluntary registry, chromosomal anomalies were not always reported by the individual practitioners so certain data points were lost to collection.

DiGeorge anomaly, which belongs to the spectrum of 22q11 deletions, is characterized by congenital immunodeficiency with increased susceptibility to infections, abnormal facies, congenital heart defects, hypoparathyroidism with hypocalcemia, and cognitive/ psychiatric problems1. Pathological findings of DiGeorge syndrome may include abnormalities of the thymus, absent or hypoplastic thymus, and absence of parathyroid glands. The failure of an embryological field derived from neural crest cells causes this constellation of defects1. Conditions associated with DiGeorge Syndrome are the other 22q11 deletion syndromes, velocardiofacial syndrome, conotruncal anomaly face syndrome, Cayler syndrome, Optic GBBB syndrome, and CHARGE syndrome. Immunologic consequences of this microdeletion stem from the impaired T cell production and function, as well as impaired humoral function. Infants presenting for cardiac surgery are at risk for developing transfusion associated graft versus host disease with a mortality approaching 100% if non irradiated blood is administered.

22q11.2 deletion syndrome affects nearly 1 in 3000 children making it the most common microdeletion syndrome. The current gold standard for making this diagnosis is the fluorescent in situ hybridization (FISH) at mononuclear white cells. This expensive test has a turn around time of 4-5 days and a false negative rate of 2%. Multiplex ligation dependent probe amplification (MLPA) can detect deletions in the 22q11. Polymeerase chain reaction can also screen for 22q11 deletions and provide a cost effective and faster way to screen a large number of at risk patients. Other time saving screening tests that can be used in this patient population include measuring the mean platelet volume from a full blood count. The mean MPV in patients with 22q11 syndrome higher than 10 fl carries an 80% test sensitivity. Practitioners can use this in situations where rapid decision making is needed for the ordering of irradiated blood products to potentially prevent fatal GVHD. Transfusion related graft versus host disease (TA-GVHD) carries a high mortality rate and is a potentially serious but preventable iatrogenic disease. On average neonates present with this disease 28 days after transfusion with fever, rash, diarrhea, hepatitis, and pancytopenia. Mortality typically occurs 51 days after the initial transfusion. Whole blood, packed red blood cells, granulocyte transfusions, and platelets have the greatest white cell loads and thus carry the greatest risks.

Congenital immunodeficiency carries a high risk for TA-GVHD especially in children DiGeorge and 22q11 syndromes. These children comprise a core group of patients that require irradiated blood. Children with DiGeorge and 22q11 deletion syndromes can have an 80% reduction in T cell function. The debate over which patients should receive irradiated blood products is largely determined by institutional practice and experience. However, patients with documented, suspected, or probable immunodeficiency must receive irradiated blood products. Most, as any collected donor directed blood, are major organ transplant hospitals who will provide irradiated blood for children up to 6 months of age, bone marrow transplant recipients, children diagnosed with malignancies, those with a known diagnosis of immunodeficiency, and various solid organ transplantations. 

References

6. www.yale.edu/imaging/chd/e_vsd/index.htm
7. Medscape-Immunology.blogspot.com/2011/05/digeorge-syndrome-22q11-del.html

Department of Pediatric Anesthesiology, Texas Children’s Hospital, Baylor College of Medicine, Houston, Texas, USA

Figure 1
Proportion of Chromosomal Abnormalities Reported to the STS Database for CPB Cases 1/2010-6/2011

Figure 2
Distribution by Age Group Reported to have a Chromosomal Anomaly Undergoing CPB to STS Database: 1/2010-6/2011

Figure 3
Chromosomal Anomalies for CPB Cases Reported in Society for Thoracic Surgery Congenital Heart Disease Database 1/2010-6/2011

References

6. www.yale.edu/imaging/chd/e_vsd/index.htm
7. Medscape-Immunology.blogspot.com/2011/05/digeorge-syndrome-22q11-del.html