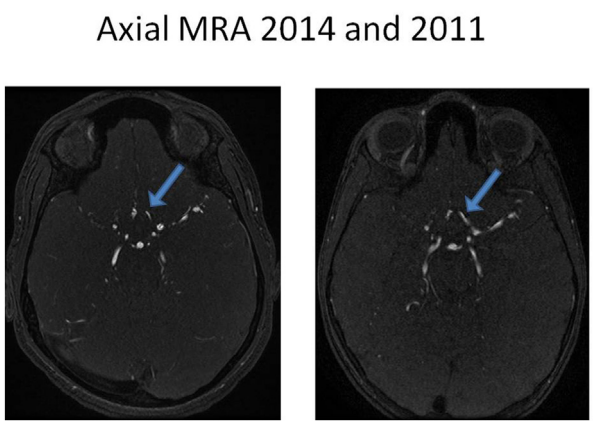


patient had a transient improvement in his vascular disease, he has now had an unexpected and significant progression. The role of sickle cell trait in his progression is unclear. Though bone marrow transplantation may be curative therapy for sickle cell disease, it may not halt the progression in all patients, especially those with severe disease.

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### Leukocyte Adhesion Deficiency Type I: The Outcome of Reduced-Intensity Conditioning Hematopoietic Stem Cell Transplantation

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**Introduction:** Leukocyte adhesion deficiency type I(LAD-I) is a congenital disorder that is usually fatal during first decade of life due to recurrent life-treating bacterial infection. Allogeneic hematopoietic stem cell transplantation (HSCT) has been accepted as one of the only curative treatment for LAD-I. The conditioning regimen used for HSCT in LAD-I is still a controversial issue.

**Patients and Methods:** Between 2007 and 2014, 20 pediatric patients(12 female) with confirmed LAD-I who were referred to our center underwent HSCT. The median age at the time of diagnosis and transplantation was 11.5 months (range:1month-5years) and 24.5 months (range:4months-14years), respectively. Patients underwent HSCT from matched related donor (n=15), mismatched related or unrelated donor(n=3), unrelated fully matched donor(n=1) and haploidentical relative donor(n=1). Sources of stem cells were peripheral blood(n=10), bone marrow(n=8) and cord blood(n=2). All patients were admitted several times due to infection, prior to HSCT. The study utilized reduced-intensity conditioning(RIC) regimen consisting of Fludarabine, Melphalan and ATG. Cyclosporine and Methylprednisolone were used as graft-versus-host disease (GvHD) prophylaxis regimen.

**Result:** All but one patient engrafted. The median time for ANC and platelet engraftment was 12 days (range: 10-23days) and 15 days (range: 10-32days), respectively. With a median follow-up of 43 months (range: 6-85months), 7 patients showed acute GvHD (2 grade I-II, 5 grade III-IV), while 2 patients developed limited chronic GvHD. The 4-year OS and DFS was 80% (95%CI: 54-92%). Among 19 patients who showed engraftment, 9 with full chimerism and 7 with mixed chimerism are still alive and disease free. Five patients expired due to GvHD and infection.

**Conclusion:** As pre-transplant infections in LAD-I lead to rise in mortality rate, the use of myeloablative conditioning regimen may result in increased risk of mortality. Using less-toxic regimen with RIC seems to be highly effective and will improve manifestation of LAD-I with either full or mixed chimerism.

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### Fludarabine Combined with Myeloablative Busulfan (FluBu4) Results in Reliable Engraftment and Low Transplant-Related Mortality in Pediatric Patients

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For many years the standard conditioning regimen for children with myeloid malignancies and certain non-malignant diseases, such as sickle cell disease, was myeloablative busulfan combined with high dose cyclophosphamide. Regimen-related toxicity remains a concern, with sinusoidal obstructive syndrome (SOS) occurring in up to 28% of patients (Ozkaynak et al, BMT 1991). The substitution of fludarabine for cyclophosphamide led to less toxicity and better outcomes in adult patients (Andersson et al, BBMT 2008), but there is little data for fludarabine/myeloablative busulfan (FluBu4) in children.

We report the outcomes for 23 consecutive pediatric patients (median 7 years old, range 0-17) who underwent allogeneic BMT following FluBu4 conditioning between December 2006 and May 2014. The indications for transplant were acute leukemia (N=12), MDS/MPD (N=7), CML (N=1), and non-malignant disorders (N=3). There were 17 unrelated donors and 6 sibling donors. Stem cell sources were marrow (N=15) or cord blood (N=8). All cord blood transplants were matched at 4-6/6 HLA-loci. Marrow grafts were allele matched at 8/8 HLA-loci in 13/15 patients; 2 were 7/8 matched. The conditioning regimen consisted of once daily fludarabine 40 mg/m$^2$ (1.3 mg/kg for patients <10kg) and pharmacokinetically-adjusted busulfan targeting a CSS of 600-900 mcg/L daily on days -5 to -2. Thirteen patients at higher risk for graft failure (HLA-mismatched grafts, cord blood or non-malignant disease) received either anti-thymocyte globulin (N=8) or low dose (2-4 Gy) radiation (N=5). All patients received a calcineurin inhibitor for GVHD prophylaxis along with short-course methotrexate (N=15) or MMF (N=8) per institutional guidelines. Notable non-GVHD toxicities developed in two patients (9%). There was one case of self-limited moderate SOS. One patient experienced fatal primary graft failure that occurred after receiving an HLA-mismatched cord blood graft for PNH; all other patients (96%) engrafted neutrophils (median 14 days, range 12-26). There were no cases of idiopathic pneumonia syndrome. Acute GVHD grade II-IV developed in 4 patients (17%) at a median onset of 26 days (range 9-139 days). Two patients developed BK virus-associated hemorrhagic cystitis while on high-dose steroids for acute GVHD. The cumulative incidence of relapse at 2 years for patients transplanted for malignancy was 31%; relapse occurred at a median of 45 days post-transplant (range 22-201 days). Non-relapse mortality and overall survival at 2 years are 14% and 63%, respectively