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Transplant-Acquired Food Allergy Following Cord Blood Transplantation in Adult Patients
Takahiko Mori, Jun Kato, Sumiko Kohashi, Shinichiro Okamoto.
Division of Hematology, Keio University School of Medicine, Tokyo, Japan

Background: The development of new food allergy after allogeneic hematopoietic stem cell transplantation (transplant-acquired food allergy: Tafa) has been sporadically reported. Most of such cases were considered as the passive transfer of food allergy through allogeneic hematopoietic stem cell transplantation (HCT) from donors already allergic to specific allergens. Although cord blood donors are basically considered lacking the known food allergy, there have been some cases of TAFa following cord blood transplantation (CBT). Therefore, we have retrospectively evaluated the adult patients who developed food allergy after cord blood in a single institute.

Patients and Methods: Among the patients who underwent CBT for hematological diseases at Keio University Hospital (Tokyo, Japan), patients survived longer than 30 days after CBT with donor cell engraftment were selected from the institutional database. Medical information about food allergy was retrospectively collected from the medical records of each patient.

Results: Of the 51 evaluable patients, 3 patients experienced episodes of new food allergy, in whom food allergy was definitely diagnosed based on the results of radioallergosorbent test and/or the rety test. The characteristics of three patients at transplant are as follows: Case 1, 55-year old male with myelodysplastic syndrome; Case 2, 57-year-old male with Sezary syndrome; Case 3, 19-year-old female with aplastic anemia. All patients received CBT following fludarabine-based reduced-intensity conditioning regimens and received cyclosporine A or tacrolimus with or without short-term methotrexate for graft-versus-host disease prophylaxis. At 10 months after CBT, Case 1 developed severe reactions after ingesting egg-containing meal, including skin rash, shortness of breath, and loss of consciousness. He was successfully treated with steroid and epinephrine. At 6 months after CBT, Case 2 repeatedly experienced episodes of severe reactions after ingesting buckwheat noodle, including fever, diarrhea, vomiting, and hypotension. He was successfully treated with massive hydration. At 5 months after CBT, Case 3 repeatedly experienced gastrointestinal symptoms such as vomiting and diarrhea after ingesting egg-containing food. At each episode, she recovered without any interventions.

Conclusion: Although the incidence is low, acquisition of new food allergy has been observed within one year after CBT. By accumulating the cases, the epidemiology and clinical feature of TAFa following CBT should be further evaluated.

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Recovery of Endogenous IgG Production Following Rituximab Treatment after HSCT
Christopher Morris, Joan Morris. Pediatrics, Loma Linda University, Loma Linda, CA

Rituximab is a monoclonal antibody to the CD20 antigen expressed on B lymphocytes. Several recent reports suggest that rituximab may be used to treat complications of SCT including GVHD and EBV reactivation. The long term consequences on IgG recovery aren’t well studied. This is a retrospective analysis of allogeneic pediatric SCT patients treated with rituximab at Loma Linda University from 2004 to 2013. We treated 23 patients with rituximab following allogeneic SCT (11 MUD, 7 MSD, 3 Cord) for post-transplant EBV reactivation alone (4), cGVHD alone (4) in combination with thrombocytopenia (9), hemolysis (4) or EBV reactivation (2). During and at end of rituximab therapy all patients required IVIG monthly or more frequently (4) to maintain serum IgG levels >500mg/dl. We examined the length of time from end of rituximab therapy to recovery of endogenous IgG production. The influence of cGVHD, EBV infection, type of stem cell graft, and number of doses of rituximab, on the pace of recovery of endogenous IgG production was evaluated. Those treated for cGVHD plus any other indication (n=19) received a median of 11 doses of rituximab (range 4 to >30). Among these patients, 11 of 14 whose cGVHD resolved and came off immune suppression recovered the ability to produce IgG completely (9) or partially (2, defined as decreasing frequency of IVIG infusions to maintain IgG >500mg/dl). Mean time to recovery was 14 months (range >4 to 50 months) after last dose of rituximab.

We found no relationship between age of patient or duration of rituximab therapy on the time interval between end of rituximab therapy and onset of endogenous IgG production. Recipients of MUD grafts had a non-significant increase in failure to recover endogenous IgG production, but when the impact of therapy for cGVHD was taken into account the type of stem cell graft lost significance.

Ability to recover endogenous IgG production following treatment with rituximab after SCT depends on successful treatment of cGVHD and in this group of patients requires about 1 year from end of therapy. Among those treated with rituximab whose cGVHD does not resolve and in those with early EBV reactivation, loss of IgG production persists at least several years. In this later group, failure to recover IgG production may be due to other factors separate from rituximab therapy.

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Nitazoxanide Is Effective Therapy for Norovirus Gastroenteritis after Chemotherapy and Hematopoietic Stem Cell Transplantation (HSCT)
Joan Morris, Christopher Morris. Pediatrics, Loma Linda University, Loma Linda, CA

Norovirus is a major cause of nonbacterial gastroenteritis and is a self-limited in immunocompetent patients. However, in immune compromised pts it causes prolonged infection, GVHD and sepsis due to mucosal breakdown. Supportive care is the current therapy as attempts to treat with ribavirin or oral immunoglobulin have failed. We report our experience treating norovirus gastroenteritis occurring in 14 patients (pts) after (11) and prior (3) to HSCT with Nitazoxanide.

From Nov 2012 to Dec 2013, 14 pts (2 receiving chemotherapy, 2 auto HSCT and 10 allo HSCT) developed norovirus gastroenteritis. Ages ranged from 1 to 21 years (median 10) diagnoses included ALL (6), aplastic anemia (2), Wiskott
Norovirus was detected by RNA RT-PCR test of stool performed by Focus Diagnostics, Cypress, Ca. The dose of Nitazoxanide was 100 mg po BID for ages 1 to 4 years, 200 mg po BID for age 4 to 11 years, and 500 mg po BID for greater than 11 years. 1 pt, 33 months post allo HSCT with normal immune studies was not treated as symptoms resolved prior to test result. All other pts clinically responded with improvements in diarrhea, nausea, and abdominal pain in 2-4 days (median 2 days). 3 pts were pre-HSCT on chemo/immunotherapy and 11 were 17 days to 34 months after HSCT. All the treated pts were on immune suppression or chemotherapy. 9 allo HSCT pts were on immunosuppression and 5 of these had GVHD at onset of symptoms. Immune suppression included tacrolimus/solumedrol (3), cellcept/solumedrol (2) plus infliximab (1), tacrolimus (1), cyclosporine (1), tacrolimus/cellexcept (1). 3 pts were receiving immunotherapy (1), or chemotherapy for solid tumors (2) prior to planned HSCT. 1 pt was 10 months post auto HSCT. Clearance of stool virus was variable. 2/3 pts treated prior to HSCT became negative on stool study within 5-14 days of treatment (1 unknown duration). Among pts treated after HSCT 4/9 had persistent viral shedding, 2 received drug until death (1 adenovirus, 1 CHF) both were treated greater than 2 months, 3 with GVHD still shed virus after 6 months of treatment, and 4 are off therapy and remain negative for norovirus RNA. 1 auto HSCT pt stopped viral shedding 2 months post starting Nitazoxanide. 2 HSCT pts with clinical resolution but persistent viral shedding stopped treatment and had clinical symptoms return. These pts responded to restarting therapy within 2 days but continue to shed virus. UGI endoscopy/colonoscopy were performed in 5 pts at the time of infection, all showed inflammation/edema but no GVHD was seen on histology. Peripheral blood CD4 counts among those with persistent viral shedding ranged from 50-445/μl and for those that cleared virus 143-1222/μl.

Nitazoxanide is effective therapy for norovirus gastroenteritis in immune compromised patients. Therapy needs to be continued until stool RNA studies become negative.

Safety and Feasibility of Administering Lactobacillus Plantarum to Children Undergoing Myeloablative Hematopoietic Cell Transplantation (HCT)

Michael J. Nieder 1, Elena I. Ladas 2, Monica Bhatia 3, Michael Gates 4, Frances Hamblin 5, Aleksandra Petrovic 6, Lu Chen 7, Eric Sandler 8. 1 Blood and Marrow Transplantation, Children’s Hospital Johns Hopkins Medicine, St. Petersburg, FL; 2 Division of Pediatric Hematology/Oncology/Stem Cell Transplant, Columbia University, New York, NY; 3 Division of Pediatric Hematology, Oncology, and Stem Cell Transplantation, Department of Pediatrics, Columbia University, New York, NY; 4 Pediatric Hematology/Oncology/BMT Research, All Children’s Hospital Johns Hopkins Medicine, St. Petersburg, FL; 5 All Children’s Hospital Johns Hopkins Medicine, St. Petersburg, FL; 6 Blood and Marrow Transplant, All Children’s Hospital Johns Hopkins Medicine, St. Petersburg, FL; 7 Preventive Medicine, Children’s Oncology Group Statistical Data Center and University of Southern California, Monrovia, CA; 8 Nemours Children’s Clinic, Jacksonville, FL

Myeloblastic regimens are associated with prolonged periods of cachexia/anorexia, nausea/vomiting, mucositis, and compromised gut integrity (CGI). Studies suggest that CGI could increase the risk of developing acute Graft versus Host Disease (aGVHD). Preserving gastrointestinal integrity may decrease the risk of aGVHD which occurs in approximately 35% of children undergoing allogeneic HCT. Probiotics (nutritional supplements that contain viable microorganisms and confer a benefit to the host) have emerged as a possible therapeutic agent in preserving gut integrity. Animal studies have found that administration of probiotics reduced the incidence of aGVHD when compared to placebo. Clinical trials in children with HIV infections and adults receiving organ transplants have found probiotics to reduce morbidity and mortality. Prior to our Pilot Trial, probiotics had not been investigated in the HCT setting. This pilot study evaluated the safety and feasibility of probiotics administered to children undergoing allogeneic HCT. Patients received once daily supplementation with L.plantarum 299v (1 x 10^10 CFU/kg/day) beginning on Day − 7 and continued until Day + 14. Thirty-one patients who were undergoing myeloablative allogeneic HCT were enrolled. One patient was not evaluated for safety because only one dose was given and the patient withdrew from the study. Safety: Of 30 evaluable patients, there were no cases of Lactobacillus plantarum bacteremia (0% (0/30) with 95% exact binomial CI (0%, 12%). Feasibility: Of the 31 eligible patients, only one (#12) received < 50% of the dose. Therefore, 97% of the eligible patients (30/31), 95% CI (83-100%), received at least 50% of the probiotic dose. Clostridium difficile infections were noted in 20% of the patients by Day + 100. Non-lactobacillus bacteremia was noted in 23% of evaluable patients. Three patients died before Day + 100, but no deaths were associated with lactobacillus administration. Stage 1-3 acute gastrointestinal aGVHD was noted in 22% of patients who survived to Day + 100. The overall incidence of Grades II-III GVHD was 26%. No patients had Grade 4 GVHD. Lactobacillus plantarum can safely and feasibly be administered to children undergoing myeloablative HCT.