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We hypothesized that treatment of recipients peri-transplant with peg-mGM-CSF may be protective of GvHD and improve survival by increasing recipient Tregs. Balb/c mice (n = 5/group) were treated with peg-mGM-CSF or PBS for 4 days prior to transplantation using myeloablative conditioning and transfer of B6 splenic T-cells and bone marrow. This was followed by continued treatment with either PBS or peg-mGM-CSF for the first week after transplant. There was a trend toward worse survival in the peg-mGM-CSF treated recipients. (Log-rank (mantel-cox) test, p = 0.085) We next asked if treatment of T-cell donors might abrogate GvHD. B6 donors were treated with G-CSF, peg-mGM-CSF or PBS for 4 days, on the fifth day splenocytes were isolated and pan-T-cell selected using an AutoMACS column. An equivalent dose of CD3 + T-cells along with congenic bone marrow was administered to recipient Balb/c mice (n = 4-5/group) that had undergone myeloblative conditioning. Mice receiving GM and G treated donor T-cells had an improved survival compared to PBS alone (PBS vs. G p = 0.0314, PBS vs. GM p = 0.0467 (Log rank (Mantel cox) test)) but displayed similar GvHD scores. This effect may be explained by an increase in Tregs delivered in the G and GM group. Further studies will seek to validate these results.

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CD4$^+$ T CELLS ACCUMULATE IN THE COLON OF CSA-TREATED MICE FOLLOWING MYELOABLATIVE CONDITIONING AND SYNGENEIC BONE MARROW TRANSPLANTATION

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Syngeneic graft-versus-host disease (SGVHD) was first described as a GVHD-like syndrome that developed following syngeneic BMT and cyclosporine A (CsA) treatment. SGVHD is induced by reconstituting lethally irradiated mice with syngeneic bone marrow cells followed by a 21 day treatment with the immunosuppressive agent CsA. Clinical symptoms of the disease appear 2 to 3 weeks following cessation of CsA therapy and disease-associated inflammation occurs primarily in the colon and liver. CD4$^+$ T cells have been shown to play an important role in the inflammatory response observed in the gut of SGVHD mice. Time course studies revealed a significant increase in the migration of CD4$^+$ T cells into the colon during CsA therapy (as early as day 14 post-BMT). Significantly elevated levels of proinflammatory cytokines, chemokines and cellular adhesion molecules were observed in the colonic tissue of CsA treated animals compared to BMT controls. Homing studies revealed that a labeled CD4$^+$ T cell line, generated from SGVHD mice, migrated to a greater extent into the gut of CsA treated mice at day 21 post-BMT compared to control animals. This study demonstrates that during the 21 days of immunosuppressive therapy, functional mechanisms are in place that result in increased homing of CD4$^+$ T effector cells to the colons of CsA-treated mice.

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ATYPICAL PRESENTATION OF VAGINAL GVHD WITH ABDOMINAL PAIN CRISES

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Rare causes of abdominal pain may be overlooked in allogeneic transplant recipients with recurrent episodes of abdominal pain. We describe a 19 year-old female, who received a matched unrelated donor peripheral blood stem cell transplant for acute myeloid leukemia-M4; presenting with recurrent abdominal pain. The transplant conditioning regimen was fludarabine (125 mg/m2) and melphalan (140 mg/m2) and graft versus host disease (GvHD) prophylaxis was tacrolimus and methotrexate. The post transplant course was complicated by acute and chronic GvHD of the GI tract and skin, treated with calcineurin inhibitors, glucocorticoids, mycophenolate mofetil, sirolimus, azathioprine, extracorporeal photopheresis and narrow beam ultraviolet B (UVB). 18 months after transplantation, she presented with recurrent crises of abdominal pain. Endoscopic biopsies were negative for GI GvHD. CT scan and ultrasound of the abdomen suggested a complex 6 × 9 cm adnexal cyst arising from the left side. Diagnostic laparoscopy findings were inconsistent with a cyst. A subsequent CT of the pelvis suggested a hematocolpos. Vaginal exploration identified a transverse vaginal septum occluding menstrual flow. Transection was performed and a copious amount of blood was drained with relief of symptoms. Patient presented two months after surgery with recurrent pain and ultrasonogram demonstrated hematocolpos requiring resection of the vaginal scar tissue to alleviate the obstruction. Patient's post operative course was complicated with tubo-ovarian abscess resulting with rupture and septic shock; she underwent laparoscopic right salpingo-oophorectomy. The patient improved and was released from the hospital 2 weeks later. Biopsy of the vaginal obstruction showed a segment superficially ulcerated endocervical-type columnar mucosa and portions of fibromuscular tissue consistent with vaginal GvHD. In summary, scarring from unrecognized vaginal GvHD led to retention of menses and chronic abdominal pain. She is now using vaginal dilators with topical steroids to prevent further recurrence and clinically doing well. This case is presented to highlight awareness of this rare complication.

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NEPHROTIC SYNDROME AFTER HEMATOPOIETIC CELL TRANSPLANTATION: MANIFESTATION OF GVHD

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Although severe nephrotic syndrome (NS) has been found as a major symptom of cGVHD in murine models, the effect of GVHD on human kidney has not been studied extensively. We describe a case of NS in 16 years old female patient that was submitted to an identical sibling allo BMHSCT for CML in 1st CP. The conditioning was the BuCy regime. She received 3,8 × 10^8 mononuclear cells/kg. The GVHD prophylaxis was CSA/MTX. On D + 180, she was Phi and BCR-ABL negative and free from immunosupression without any symptons of GVHD. Five years after transplantation, she presented a cytogenetic relapse with 20% of Phi+ cells. She was treated with two DLI infusions (1.5 × 10^6 CD3+ cells/kg and 1×10^7 CD3+ cells/kg) and she became BCR-ABL negative. Until two years after the second DLI she never presented any signs or symptons of GVHD. After that, she started with intermittent urticaria and edema on the face that progress to anasarca. The clinical and laboratory investigation revealed proteinuria 2 to 8 g/24 h, hypoalbuminemia (2,3 mg/dl) and hematuria. Phi chromosome, BCR-ABL, serology for virus, syphilis and colagenosis antibodies were all negative. A kidney biopsy revealed findings of early membranous glomerulonephritis with mild mesangial proliferative glomerulopathy. The IMF confirmed granular immune deposition for IgG along the capillary loops. She was initialy treated with prednisone 1 mg/kg plus a loop diuretic and an angiotensin II receptor blocker. Secondary to steroid resistance, cyclophosphamide 1 g/m^2 plus rituximab 325 mg/m^2 for two times, in 15 days interval, was administered. Six weeks after the second cycle of Cy/Rituximab the intermittent urticaria and 8 g/24 h proteinuria were still present. Thus, the patient started CSA 5 mg/kg. After six months of CSA, the urticaria and proteinuria (170 mg/24 h) disappeared completely, and albumin reaches 3.6 mg/dl. Now, she is in a tapering regimen for CSA. NS following HSCT is a rare complication. It is mainly related to membranous nephropathy and less frequently to minimal change disease, focal segmental glomerulonephritis, diffuse proliferative glomerulonephritis or IgA nephropathy. Other renal complications of HSCT include drug and radiation toxicity and thrombotic microangiopathy that need to be ruled out in the differential diagnosis. In conclusion: the literature supports the existence of renal GVHD. However, further investigations are warrant since the pathophysiology is unclear and there is no treatment established.