HHS Public Access

Author manuscript

Bone Marrow Transplant. Author manuscript; available in PMC 2015 May 27.

Published in final edited form as:

Bone Marrow Transplant. 2008 July ; 42(1): 71–72. doi:10.1038/bmt.2008.81.

Rituximab-responsive Guillain–Barré syndrome following allogeneic hematopoietic SCT

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Guillain–Barré syndrome (GBS) is a rare complication of allogeneic hematopoietic SCT (allo-HSCT).[1,2] We describe the case of a patient who developed GBS after T-cell-depleted HSCT (TCD-HSCT) for myelodysplastic syndrome (MDS). EBV reactivation occurred concomitantly. Treatment with rituximab was associated with a marked improvement in motor function.

A 58-year-old man was diagnosed with MDS in May 2003. He was monitored without treatment for 2 years until he developed AML. Induction chemotherapy with idarubicin and cytosine arabinoside was complicated by persistent pancytopenia. Pre-transplant screening revealed that the patient was seropositive for EBV, while his HLA-identical brother donor was seronegative. In May 2006, he received a TCD-HSCT with conditioning comprised of busulfan, melphalan and fludarabine with rabbit antithymocyte globulin. The graft consisted of 13.4×10^6 CD34 cells/kg with 1.4×10^3 CD3 cells/kg. Neutrophil and megakaryocyte engraftment occurred on D+9 and D+14, respectively. No signs of GVHD occurred.

At 69 days after transplantation, he presented with a 5-day history of mid-thoracic back pain, paresthesias in the toes and fingers, and progressive symmetrical ascending motor weakness. A self-limited episode of diarrhea preceded the neurological symptoms by 1 week. On exam, motor strength was graded 2/5 in the lower extremities and 3/5 in the upper extremities. Deep tendon reflexes were absent in the lower extremities and diminished in the upper extremities. Magnetic resonance imaging of the brain and spine was normal. Cerebrospinal fluid had a normal glucose concentration of 84 g per 100 ml, an elevated protein content of 144mg per 100 ml, and one white cell per μl. Gram staining, India ink staining, culture and PCR detection for varicella-zoster virus, cytomegalovirus and herpes simplex virus were all negative. Tests for *Campylobacter jejunii* were negative. Electromyography and nerve conduction studies showed a severe and acute axonal process affecting only motor nerves and consistent with the acute motor axonal neuropathy (AMAN) type of GBS. He received i.v. Ig 500 mg/kg/day for four consecutive days, but nonetheless developed quadriplegia, dysautonomia and respiratory failure, requiring mechanical ventilation. One month later a second course of i.v. Ig was administered, at same dose, again for four consecutive days, but yielded no clinical improvement.

At 40 days after developing neurological signs, the patient was found to have EBV viremia by quantitative PCR (9673 EBV genome copies/ml). Computed tomography of the neck, chest, abdomen and pelvis showed no evidence of post-transplant lymphoproliferative disease (PTLD). He was given rituximab (375 mg/m^2) once a week for 4 weeks, resulting not only in resolution of EBV viremia by quantitative PCR but also in a significant improvement in his muscle strength. After the second dose of rituximab, his muscle strength in the upper extremity was grade 3/5 and by the end of the fourth dose further improved to grade 4/5. He was extubated without further need for ventilatory assistance. At 9 months after HSCT, the patient was diagnosed with gastrointestinal GVHD, responsive to steroids. He is now 20 months after HSCT, ambulating with the assistance of a walker.

GBS is an idiopathic acute inflammatory demyelinating polyradiculoneuropathy characterized by progressive weakness, areflexia and sensory abnormalities.[3] It is generally believed to result from aberrant humoral and cellular responses directed against peripheral nerve components. There have been several reports of GBS following HSCT, but it is unclear whether these associations occur by chance, whether HSCT predisposes patients to developing GBS or if GBS presents as a form of GVHD. GBS occurring in the early post-transplant period has been attributed to the conditioning regimen, particularly to cytosine arabinoside.[2,4] Our patient developed GBS 69 days after allo-HSCT, arguing against a chemotherapy-induced neuropathy. It is more frequent after allo-HSCT, with 26 reported cases, including our patient, compared to 7 cases after autologous HSCT.[4,5]

Despite therapy, about 25% of patients with GBS require mechanical ventilation, up to 15% die and 20% are left disabled. The prognosis of patients who develop GBS after allo-HSCT is particularly poor, with a mortality rate of 34%. Treatment is aimed at the pathogenic antibodies that target peripheral nerve tissues, either by using i.v. Ig or plasma exchange.[3] Two-thirds of patients report an infection prior to diagnosis of GBS. Our patient had symptoms of diarrhea preceding the onset of GBS. It is possible that an underlying infection might have elicited an immune response leading to GBS, although investigations failed to detect a viral or bacterial infection. He received a TCD allograft and ATG as part of his conditioning regimen, both of which were risk factors for EBV reactivation,[6] detected in this patient several weeks after the onset of GBS symptoms.

To prevent PTLD, our patient received rituximab therapy, resulting in clearance of detectable EBV viremia and marked improvement in motor neuropathy refractory to two courses of i.v. Ig. Rituximab is a chimeric monoclonal antibody that targets CD20. It has been successfully used in chronic neuropathies,[7] but its use in GBS has not previously been described. AMAN, one of the subtypes of GBS, has been linked to several antiganglioside antibodies that damage axons at the node of Ranvier or at the nerve terminals.[3] Rituximab may be beneficial in GBS, especially in the AMAN subtype, by removing pathogenic B-cell clones and thereby preventing axon damage by antiganglioside antibodies.

The reported incidence of GVHD among patients who develop GBS is 73%. In some patients, the course of GBS and GVHD seemed to run in parallel, with an improvement in the neuropathy only after GVHD control.[4] Patients with chronic GVHD are more likely to develop autoantibodies,[8] and GVHD has been associated with several autoimmune disorders

of the peripheral nervous system.[9] Furthermore, rituximab therapy has been identified as beneficial in patients with steroid-refractory chronic GVHD.[10] It is therefore conceivable that GBS in our patient was a manifestation of GVHD.

In conclusion, the prognosis of GBS occurring after allo- HSCT is particularly unfavorable. The association between HSCT and GBS is likely not coincidental, but it remains to be seen if immunologic dysregulation associated with HSCT predisposes to the development of GBS from autologous B cells, or if GBS is a manifestation of GVHD caused by donor-derived alloreactive B cells. The neurological improvement following rituximab administration to our patient may be of interest to physicians treating GBS refractory to standard therapies.

Acknowledgements

This study was supported in part by The Marrow Foundation 1K04-01 (KCH) and National Institutes of Health Grant HL070053 (KCH).

References

1. Wen PY, Alyea EP, Simon D, Herbst RS, Soiffer RJ, Antin JH. Guillain–Barré syndrome following allogeneic bone marrow transplantation. Neurology. 1997; 49:1711–1714. [PubMed: 9409375]
2. Rodriguez V, Kuehnle I, Heslop HE, Khan S, Krance RA. Guillain–Barré syndrome after allogeneic hematopoietic stem cell transplantation. Bone Marrow Transplant. 2002; 29:515–517. [PubMed: 11960272]
3. Hughes RA, Cornblath DR. Guillain–Barré syndrome. Lancet. 2005; 366:1653–1666. [PubMed: 16271648]
4. Amato AA, Barohn RJ, Sahenk Z, Tutschka PJ, Mendell JR. Polyneuropathy complicating bone marrow and solid organ transplantation. Neurology. 1993; 43:1513–1518. [PubMed: 8394521]
5. Bashir RM, Bierman P, McComb R. Inflammatory peripheral neuropathy following high dose chemotherapy and autologous bone marrow transplantation. Bone Marrow Transplant. 1992; 10:305–306. [PubMed: 1330151]
6. Gross TG, Steinbuch M, DeFor T, Shapiro RS, McGlave P, Ramsay NK, et al. B cell lymphoproliferative disorders following hematopoietic stem cell transplantation: risk factors, treatment and outcome. Bone Marrow Transplant. 1999; 23:251–258. [PubMed: 10084256]
7. Nobile-Orazio E. Treatment of dys-immune neuropathies. J Neurol. 2005; 252:385–395. [PubMed: 15834625]
8. Patriarca F, Skert C, Sperotto A, Zaja F, Falleti E, Mestroni R, et al. The development of autoantibodies after allogeneic stem cell transplantation is related with chronic graft-vs-host disease and immune recovery. Exp Hematol. 2006; 34:389–396. [PubMed: 16543073]
9. Patchell RA. Neurological complications of organ transplantation. Ann Neurol. 1994; 36:688–703. [PubMed: 7979215]
10. Cutler C, Miklos D, Kim HT, Treister N, Woo SB, Bienfang D, et al. Rituximab for steroid-refractory chronic graft-versus-host disease. Blood. 2006; 108:756–762. [PubMed: 16551963]